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ROENTGEN-RAY FINDINGS AND THE CLINICAL BACKGROUND*

CALDWELL LECTURE, 1932

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KALAMAZOO, MICHIGAN

INTRODUCTORY REMARKS

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As we assemble for the thirteenth time to pay our respects to the memory of one of the members of this Society who made outstanding contributions to the development of medical roentgenology, it is fitting that for a few moments we recall the origin of this event and why Eugene Wilson Caldwell's name was chosen to designate the annual lecture. I find many among our members unacquainted with the importance of Caldwell's work, unaware of the fact he was one of the martyrs to the ignorance of the early workers of the dangers attending the use of the roentgen rays, and that he died in military service. And yet it is not surprising that these things should not be generally known, for since the passing of this distinguished roentgenological leader there have been added to this Society's roll the names of approximately two hundred new members, the majority of whom never had the privilege of seeing or knowing or of receiving inspiration from personal contact with this man who did so much to develop modern roentgenological apparatus and to place the practice of roentgen diagnosis and therapy upon a high plane as a medical specialty.

The late Preston M. Hickey, whose own life and works with equal justice merit a lasting memorial, gave the Caldwell Lecture of 1928. This address was devoted to the story of the life of Eugene Caldwell, a description of his contributions toward the conquest of the many mechanical and technical difficulties which beset the earlier workers, and pointed out the fact that there were a number of illustrious American pioneers in roentgenology to whom every member of this Society is indebted. The choice of the name of Caldwell to serve as a representative of these pioneers came about in this manner:

On numerous occasions, when listening to our best teachers attempting to expound in fifteen or twenty minutes a valuable lesson which by lack of adequate time was set forth only fragmentarily and hastily, there came to me, as no doubt it has to all of you, that it would be a wonderful thing to give at least one speaker of each year all the time desired, without the interruption of gavel or gong, to deliver his complete lesson in sufficient detail and rounded fullness to make it a satisfaction both to orator and to auditors. Only last night, as we listened to a distinguished physicist speaking from this platform, we realized how delightful this could be. It is the usual practice in our meetings to limit the speakers to a certain few minutes, and they seldom fail to show it by too rapid delivery, spotty selections from their prepared paper, with a certain nervousness betraying their evident intention to comply with the president's injunction not to overrun the allotted

* The thirteenth Caldwell Lecture, delivered at the Thirty-third Annual Meeting, American Roentgen Ray Society, Detroit, Mich., Sept. 27–30, 1932.

time. When this Society honored me with its highest office and it devolved upon me to arrange the program and preside over the Minneapolis meeting in 1920, I realized that at last I had it in my power to experiment with such a number for the program. Accordingly, after consultation with other officers, including particularly Dr. Hickey, and because of the close personal friendship with which Dr. Caldwell had honored me, I decided to put on a formal lecture, termed the Caldwell Lecture, which I trusted would turn out so well the Society would perpetuate it by making it an annual event.

We had been back from France something over a year, with the momentous events of the World War still vividly fresh in our memories. I recalled the numerous visits I had made to Caldwell's bedside in December and January of 1917 and 1918, for I was sent back from France to assist in better correlation of the military roentgenological service here with that in the American Expeditionary Forces. On various occasions I found myself in New York at a time when Caldwell was in the Memorial Hospital undergoing a series of surgical interventions in the attempt to hold back the approach of the Grim Reaper. Like many of the other pioneers, Caldwell had been ignorant of the dangers attending the use of the roentgen rays until his early work had already developed serious damage to his hands; the insidious advances of malignant disease resulting from these early injuries brought him to his final illness in 1918, the end on the twentieth day of June being the culmination of many months of almost continuous suffering. My days in New York were full of the duties of my mission, but, as Caldwell's sufferings respected no regulations as to visitors, I used to visit him as often as possible to keep him company in some of his midnight hours. I came to realize his devotion to the success of our belated military efforts, for he was constantly pondering over the solution of some of the problems to which he had been assigned, particularly the stereofluoroscope, now nearing perfection. Hence it was that in naming the annual lecture which we hoped to see established, we chose the name of Caldwell. His accomplishments in roentgenology are so numerous that it would be unwise to take the time to recall them now. Let me suggest that those of you who did not hear Hickey's lecture of four years ago, will find pleasure and inspiration in looking back in your files of the *American Journal of Roentgenology and Radium Therapy* to the Hickey Memorial Number, February, 1931, to read the Hickey Caldwell Lecture.

For the first Caldwell Lecturer, I selected Walter C. Alvarez, then of San Francisco, now of the Mayo Clinic, who talked on "Peristalsis in Health and Disease." This lecture was published in our Journal, and later in book form, and still later revised as an excellent introduction to gastroenterology. The lecture was a great success and the Society voted to make it a permanent item of future programs.

Subsequent lecturers, like Alvarez, have maintained high standards, the occasion being made the most dignified and serious hour of our annual meeting, a matter of considerable personal gratification to its originator who in instituting the memorial to Caldwell builded better than he realized.

Let me pass in rapid review the now imposing list of Caldwell Lecturers:

After Alvarez came Dr. René Ledoux-Lebard, head of the X-Ray Department at the famous Hôpital Salpetrière, an important consultant in the Radium Institute and occupant of the first chair of radiology established by the University of Paris. This distinguished Frenchman also contributed mightily to the success of the roentgenological service, not only of the French military establishment, but also to the training of United States Army medical officers destined for roentgenological service in France. These officers, already prepared by a tour of duty in the schools of instruction in military roentgenology conducted by Manges, LeWald, Stewart, Baetjer, Gray, Skinner, Blaine, George and others, were found still in need of practical exercise in certain field methods which could only be furnished in the field; so we established three "finishing schools," so to speak, one in Paris under Dr. Hickey, one in Bazouilles-sur-Meuse under Dr. Bowman, and the third one in Tours under Dr. Ledoux-Lebard with our Captain Lindsay in military command. In this school at Tours, Ledoux-Lebard was able to render conspicuous service by finishing the preparation of scores of our officers for appointment to mobile surgical and evacuation hospitals. In addition, his monograph on the localization and extraction of foreign bodies of war became a classic in several languages. It was therefore highly fitting that our Society should have invited this eminent French roentgen-

ologist to deliver the second Caldwell Lecture. The dissertation on deep roentgen therapy was amplified into a small monograph finally published in French.

Three other distinguished foreign roentgenologists have honored us by accepting the invitation to deliver the Caldwell Lecture: Professor Forssell of Stockholm, head of the Radiumhemmet, member of the Medical Committee for the Nobel Prize, recognized as dean of radiologists in Scandinavia, who talked on experiences relating to the permanency of radiological cure in cancer; Professor Kaye of London, internationally known physicist, head of the National Physical Laboratory at Teddington, a man who has done so much to develop our knowledge of roentgen and radium physics and biology, who discoursed on "Some Fundamental Aspects of Roentgen Rays and the Protection of the Roentgen-Ray Worker"; and Professor Haenisch of Hamburg, one of Germany's giants in roentgenology, whose name, familiar to members of our Society and to readers of our Journal, will always be linked with the story of the development of urologic and intestinal roentgenology. Professor Haenisch was with us here in Detroit in 1910 at our meeting in the old Cadillac Hotel, and again last year at Atlantic City where he gave the Caldwell Lecture on "Roentgenology as a Specialty."

The remaining lectures were delivered by able and distinguished Americans: Dr. P. M. Hickey, already referred to; Dr. Percy Brown, perhaps the most intimate and devoted friend of Caldwell among our membership, on "Medical Education in its Relation to Roentgenology"; Dr. William Duane, the distinguished physicist, of the Huntington Memorial Institute for Cancer Research, Boston, on "The Scientific Basis of Short Wave-Length Therapy"; Dr. James Ewing of New York, the illustrious clinical pathologist who as leader of the group of eminent workers at the Memorial Hospital, has done so much for the development of our knowledge of the physics, biology and clinical applications of radiant energy to the cancer problem, on "Tissue Reaction to Radiation"; Dr. T. Wingate Todd of Cleveland, well known as a teacher and investigator in anatomy, on "The Rôle of Roentgenology in Medical Education"; Dr. Frederick Baetjer of Baltimore, one of America's most eminent roentgenological pioneers, a leader in roentgenological education, on "The Teaching of Roentgenology"; and Dr. W. D. Coolidge, so well known to all of us for his numerous achievements in physical research, for his aid in relieving the inconveniences of a daily incessant battle with gas tubes, mechanical interrupters, and other annoyances of the roentgenological practice of twenty years ago not familiar to many roentgenologists of today. Dr. Coolidge, who also made notable contributions to the perfecting of roentgenological apparatus for war work, lectured on "The Development of Modern Roentgen-Ray Generating Apparatus."

The twelve scientists who thus far have been asked to honor us on the occasion of the Caldwell Memorial Lecture, have with one exception elected to speak on the physical, the therapeutic and the educational aspects of roentgenology. Alvarez gave an important clinical, diagnostic and physiological paper, and part of Hickey's lecture dealt with the clinical applications of some of Caldwell's work in a field in which Hickey himself had accomplished notable success. The mechanical and the pedagogic side of roentgenology is of great moment, and familiarity with the physical side is essential as a preliminary to the most effective use of the roentgen rays as a diagnostic means, a preliminary not sufficiently recognized by the rank and file of the medical profession, today all too willing and ready to assume the rôle of roentgen diagnosticians. The clinical applications of the modality with which we work must not be neglected. After all, as physicians, we are most interested in the practical applications of roentgen rays to diagnostic and therapeutic problems.

Tonight we shall hear the message of one who may be considered to represent the ideal in a roentgenological specialist, a physician who has all along maintained his standing and efficiency as a clinical diagnostician and practitioner of the healing art while developing superior skill in the application of the roentgen rays to medical problems. There is a definite tendency for the specialist in diagnostic roentgenology to be looked upon as an exalted assistant somewhat of the nature of a photographer, a fate invited by many who look upon their work as an affair of pictures without much importance being attached to the fluoroscopic and clinical aspects of their professional endeavor. We should first of all be physicians, physicians practising roentgenology. Michigan has in its roentgenological ranks a man who in the fullest sense exemplifies

this idea, the speaker of the evening, a man whose works have made a name for him throughout the civilized world, whose personal characteristics have endeared him without exception to all with whom he comes in contact, whose personal knowledge of and friendship with Caldwell qualifies him in a high degree for the lecture to which we are about to listen. It gives me great pleasure to call upon Dr. Augustus W. Crane, who has chosen as his subject "Roentgen-Ray Findings and the Clinical Background."

CALDWELL LECTURE

DR. CASE'S eloquent tribute to the character and achievements of Eugene Caldwell leaves nothing to add except a brief personal word of appreciation. To me he exemplified the best traditions of this Society. He combined ability with modesty, dignity with friendliness, invention and research with the routine of daily practice, judgment and restraint with unfailing enthusiasm, a retiring disposition with innate qualities of leadership, and an undiminished zest for his life work with courageous resignation finally to meet an untimely end. In Eugene Caldwell we typify the martyrs of pioneer roentgenology in America and erect his name in these Lectures as a monument to our honored dead.

The subject of the present lecture is closely related to one of the most significant events of Caldwell's life. Entering the field of roentgenology as an electrical engineer and possessing unrivaled skill in the technique of the roentgen ray, yet in the midst of a brilliant professional career Caldwell paused to enter a school of medicine and to add an M.D. degree to his other titles of distinction. Nowhere in the annals of roentgenology is there a finer example of fidelity to an ideal. This act framed in unequivocal terms his mature conclusion that a medical education is essential to the roentgen diagnostician; that the best insight and judgment of the trained roentgenologist require the clinical background. One of my most cherished recollections is a visit of Caldwell to our office when his chief interest was not in apparatus or plates but in our reports where the roentgen examination was embodied along with the history and the assembled clinical findings of each case. It is on the basis of this work and as a tribute to the medical education of Eugene Caldwell that I choose the subject "Roentgen-Ray Findings and the Clinical Background."

The practical roentgenologist may suspect that this title conceals the roentgenological idealism of one who has never been up against the hard daily facts of hospital practice. In reality it covers many years' experience of a fellow workman who has watched the roentgenologist evolve from clinician to specialist and from specialist to technician, and who hopes to see his feet once again planted firmly on the ground of clinical roentgenology. This subject is peculiarly entangled with the professional standing of the roentgenologist, his education, proper function, duties, rights, privileges and future. Haenisch, in the last Caldwell Lecture, discussed these questions with profound knowledge and philosophic insight. While we will not enter directly into this discussion, yet as we develop our subject, these same questions will be seen to pursue us like shadows.

At the outset we recognize that in a general roentgenological practice there is a daily run of technical work where the clinical background is of little or no importance to the roentgenologist. Such are fractures, dislocations, foreign bodies and those cases where the physician, surgeon or specialist specifically asks for a roentgen report which is yes-or-no regarding, for example, urinary stone, pathological gallbladder, large thymus, size of heart, aneurysm, filling of antrum or mastoid, etc. This, in the minds of many of our clinical confrères, is the ideal type of report and in some hospitals and clinics is called for in nearly all kinds

of cases. It assumes that a roentgen report can be made and added to the clinical charts along with the blood count and the urinalysis. It fills the requirements particularly of hospitals and permits quantity production. At a certain hour of the morning we see the roentgenologist before a stack of films with an assistant on one side and a stenographer on the other. With incredible rapidity he passes one film after another before the viewing box. A word, a crisp sentence, rarely more; occasionally a pause for a series of films; occasionally an order for more films to be made in a case, and the work speeds on. We may admire the executive ability, the mobilization of experience and the sureness of the interpretations. A big business man or his efficiency expert will admire it still more.

In another room, perhaps in the same hospital, we may see a different picture, a prophetic corollary to the first. Perhaps it is a urologist before his staff, with visiting physicians and students, running through his cases at a morning conference. A case-history is read and discussed—symptoms, laboratory analyses, cystoscopic tests. Then roentgen films are shown—abdomen, pyelograms, ureters, and bladder. In the light of the whole case the interpretation is made, the diagnosis formulated, and the factors bearing on treatment considered. This you say is not the conference of a roentgenologist but of a clinician. Exactly so. It shows that clinical roentgenology in some quarters is passing out of the hands of the roentgenologist into the hands of the clinician. Many years ago in a published paper, I stated that if the roentgenologist did not remain a clinician, the clinician would become the roentgenologist. We thus see quantity production without clinical background; and again in contrast, interpretation without the roentgenologist. It may well puzzle the wisest to see how the roentgenologist under present-day conditions can combine clinical with roentgenologic interpretation. And many may doubt the logic or the wisdom of an attempt to do so.

Two postulates may be made:

First, that the roentgenologist should plan his own roentgen examination.

Second, that the roentgenologist should interpret his own film and screen findings.

These postulates seem too obvious to require formal statement or proof. Both unquestionably are accepted in principle but unthinkingly ignored in practice by both physician and roentgenologist. If the roentgenologist is to plan the examination, then he must know about the case, the clinical background, the present condition of the patient, the diagnostic problem to be solved. When the roentgenologist is his own technician and comes in immediate contact with the patient, as is usually the case in a small private practice or to a limited extent even in a large hospital service, then some clinical features are at once manifest, such as the sex, age, nutrition, general condition. A moment's questioning as the patient is laid on the table or stands behind a fluroscopic screen may add much to the understanding of the case. But why such indirection, such a furtive effort to obtain needed information? Why not regularly have the clinical record accompany the case, and make any clinical examination which may be required to comprehend the diagnostic problem and to plan the roentgen examination? The planning may be merely a decision as to what organ to examine or what signs to look for. It may be a matter of sequence, as for example, the examination of the renal tract, urographic or cystoscopic before barium is given; or it may mean a careful scrutiny of the clinical background to find the best point of roentgen attack.

As we shall show, there may be multiple pathology present either as separate coincident diseases or as links in an evolutionary chain of a single disease process; or, there may be a possible reflex syndrome; or, again, the symptom-complex of a disease above the diaphragm may involve organs below, with negative findings to perplex and annoy. Rare conditions in the aggregate may equal in numbers any single common condition. Intelligent planning of the

examination enables us to avoid pitfalls, detours, and lanes that lead nowhere. The more accurately we can focus the roentgen ray on the clinical map, the better we can show the way.

It is easy to overlook plain evidence in films or on the screen if the case is not understood. It is no uncommon experience after operation or autopsy for the roentgenologist to re-examine his films and see informative details that had escaped his eye. How many of us have defended the roentgen ray by explaining how this or that condition could have been demonstrated "if we had known." It is a preliminary knowledge of the clinical background that makes the roentgenologist alert for clues and signs, alive to significant evidence that might otherwise seem irrelevant and immaterial. This is one reason why the responsible roentgenologist can rarely delegate to an assistant the fluoroscopic examination. With a patient under screen inspection and palpation, the roentgenologist is a true clinician. It is at such a time that he can best realize that the roentgen examination is an integral part of the physical examination, and not a method to supplant it. It is an extension of vision; but such is the importance of the eye and such the supremacy of things seen, that the x-ray revelation may blind us to the fundamental document of the case, which is the clinical history.

In the recent hospital work of a friend, a case was sent for roentgen examination to determine the presence or absence of a pathological gallbladder. It was a yes-or-no order specifying and limiting the examination. This is not a hypothetical example but an actual occurrence. I was present. Fortunately, the attending surgeon came in and an impromptu consultation resulted. The history and symptoms were run over briefly and the physical examination repeated in part, as the patient lay on the x-ray table.

"Can you stand up"? the patient was asked.

"Sure," he answered, "I am not as bad off as you fellows think."

In a few moments he was behind the upright screen and we saw a true pathognomonic roentgen sign, a thin but distinct layer of gas beneath the right diaphragm. A film was exposed for a hospital record and the case at once sent to the operating room with the diagnosis of a perforation somewhere in the gastrointestinal tract, almost certainly in the duodenal bulb, because this is the common location in patients not in collapse and because the correlation of clinical data indicated this site. Needless to say, a perforating duodenal ulcer was found by the surgeon and the patient made the stereotyped "uneventful recovery." It is safe to assume that if this case had fallen into the hands of a technician who had followed his yes-or-no order, the operative hazard would not have been kept at a minimum. Even if the diagnosis had been established by the barium method, it would have been a departure from the definite order to the roentgenologist; moreover, barium even in small quantities may be undesirable in the peritoneal cavity. As well have the internist plan the operation for the surgeon as the surgeon plan the examination for the roentgenologist.

We may take a hypothetical case, which, with many of you perhaps has been duplicated repeatedly. Let it be one of suspected intestinal obstruction and let the order read for roentgen examination by barium meal and enema. This is definite, and to most surgeons would seem an intelligent and reasonable order. A technician would save time, trouble, explanations and questions about charges, by proceeding with the examination as planned for him. But a roentgenologist considers the best solution of the diagnostic problem. He knows that if the case is one of acute obstruction then barium may obscure the picture. An order does not relieve him of responsibilities. He must know if inflammatory conditions have been excluded. Assuming that the case has been carefully examined and diagnostic possibilities considered, this does not help the roentgenologist unless he has been in consultation with the surgeon, which is un-

likely in busy hospital or private practice. Moreover, diagnostic hypotheses do not, as a rule, appear on hospital charts, and clinical records do not commonly accompany private patients. The roentgenologist needs his medical education. A roentgen examination is a consultation and the privilege of a clinical examination is inherent. It takes but little time to learn that the clinical background is indeed that of acute obstruction, and at the same time we have learned perhaps the essentials of the differential diagnosis of the case.

The original order, of course, may be diplomatically disregarded and plates made in the prone and upright positions. If the patient is too ill to sit upright, then a plate may be made in the lateral position to show fluid levels. If these plates show gaseous distention of loops of the small intestine, every roentgenologist knows that a diagnosis of acute small intestinal obstruction may be made. If fluid levels are found in these loops he knows the prognosis is less favorable. If the gas distention is all in the stomach and duodenum, then acute dilatation of the stomach with traction obstruction of the duodenum is to be considered. The duodenum may show no gas except in the supine position. In the other positions, fluid may obscure the lower stomach and duodenum. In acute dilatation of the stomach, the stomach tube is frequently passed to relieve the pressure, and a barium mixture may be poured in to delineate that portion of the stomach and duodenum obscured by fluid. In case of gas-distended small intestine, the barium enema is commonly used as a safeguard in differentiating colonic gas distention and, of course, furnishes the answer to questions of colonic obstruction. The above points are enumerated to illustrate problems of the roentgen-ray examination known to the roentgenologist but are not as a rule considered by the physician who gives the order for a roentgen examination.

Partial obstruction of the small intestine may not give the clear-cut pictures described and may elude positive diagnosis, even with the barium meal. Ulcer of the duodenum with very marked contraction of the lumen may nevertheless be attended by gastric hyperperistalsis and rapid expulsion exactly as in ulcer of the bulb, whereas in cancer of the duodenum, without much narrowing of the caliber of the intestine, there may be a wide patulous pylorus with a two-, three- or four-day retention without gastric dilatation. The behavior of the stomach cannot be disregarded in those cases which do not give the pathognomonic signs of obstruction. These cases are cited to enforce the dictum that the physician or surgeon should state the diagnostic problem and give the provisional diagnosis, but that the roentgenologist should plan the roentgen examination.

We believe that the surgeon, internist, physician or specialist is perfectly willing to state the problem and that when the plan of the roentgen examination is ordered, it is merely an effort to make plain what is wanted of the roentgenologist. It is manifestly within the prerogative of the roentgenologist to design the roentgen-ray order blank. Let it contain a space for "Diagnostic Problem" and a second space for "Provisional Diagnosis." At the bottom of the blank let there be a note to the nurse, "Have clinical charts accompany patient." The roentgenologist will then better realize why a general medical education should be required to practice roentgenology, and his medical associates will more clearly appreciate the true nature and scope of his services.

PATHOGNOMONIC SIGNS

The foregoing cases show several pathognomonic signs—the subphrenic gas zone of acute perforation, the small intestine distention of acute obstruction, the gas distention of acute dilatation of the stomach, and the prolonged gastric residue of duodenal cancer without obstruction. The roentgen ray has produced more pathognomonic signs in a few years than clinical observation brought forth in centuries. Neverthe-

less, the roentgenologist will find his diagnostic powers greatly enhanced by a ready familiarity with the tested clinical signs which the years have sifted out of the accumulated experience of the past masters of medicine. It is a form of diagnostic culture that improves the judgment and pays in personal satisfaction. A clinically minded roentgenologist may see many things that cannot be developed in the dark-room, although he may not be able to match the following example of the recognition of a disease by a pathognomonic sign.

Corrigan was passing through the wards of a London hospital with a professional friend. He saw a patient's foot protruding from under the bed covers and noted the movements of the foot with each heart beat. He perceived at a glance the water-hammer pulse that has since borne his name and remarked in passing that this patient had an aortic regurgitation and a bovine heart. "Correct," said his friend, "but how did *you* know?"

The combination of a leading symptom with a supporting sign is an approach to the symptom-complex which may have very nearly the force of a pathognomonic sign. A study of a symptom-group may show the roentgenologist how best to add a roentgen sign that will certify the diagnosis. The laboratory provides examples of this type of achievement. The symptom-complex of diabetes is progressive loss of weight and strength, hunger, thirst, and polyuria. The laboratory added the finding of sugar in the urine and the diagnosis became definite. Nephritis is another familiar example. When Bright first demonstrated albuminuria, he added to the symptom-complex of nephritis a sign which is still pathognomonic if sufficiently guarded. The microscopic picture raised the anemias and leucemias from symptomatic obscurity to clear-cut definition.

Clinical instrumentation may supply the decisive sign. The syndrome of hyperthyroidism is rapid pulse, nervousness, loss in weight, goiter, slight afternoon rise of temperature, tremor and perhaps exophthalmos. One or more of these may be lacking and the clinical picture seem out of focus. But the estimation of the basal metabolism introduced the pathognomonic factor. In certain cardiac syndromes, particularly in coronary thrombosis, a similar service has been performed by the electrocardiograph. In other lines but in essentially the same way the roentgen ray has gained greater victories over a wider front.

The demonstration of gallstones completes the symptom-complex of cholecystitis. The filling of the anterior mediastinum does the same for the symptom-complex of large thymus. But nowhere over this long front where diagnostic forces are engaged in the ceaseless battle with disease is there a more brilliant and successful example than that of the roentgen ray with duodenal ulcer. That disease is in progress is seen in the symptom-complex; epigastric pain coming on from one to three hours after meals, relieved temporarily by eating or alkalies, accompanied by hyperacidity of the gastric juice, and at times by blood in stools or vomitus. When the roentgen ray is brought into action we find a constant deformity of the duodenal bulb by the rapid-fire serial plate method—thanks to the genius of Lewis Gregory Cole. Every roentgenologist the world over knows this and makes the diagnosis of duodenal ulcer with the certainty and security of the clinician who makes the diagnosis of pulmonary tuberculosis after finding tubercle bacilli in the sputum.

Most brilliant successes carry with them potential dangers. The present case is no exception. It has set an example for other roentgen work. Why, his associates ask, should not all roentgen examinations as they become more perfect, conform to this model? There is nothing, they say, about the roentgen demonstration of a pathological gallbladder or a duodenal ulcer that a technician cannot do and does not do. What then ultimately will be the need of a roentgenologist with an expensive medical education? Will the "pure" roentgenologist, by his own research and the perfecting

of his technique, eliminate himself? Rather, he may discover himself reborn in the internist who is himself becoming a clinical roentgenologist.

That the syndrome of duodenal ulcer was at first insufficient for the diagnosis is clearly shown by the examination of medical literature. From the first knowledge of ulcer to the demonstration of Cole, peptic ulcer was supposed, with rare exceptions, to be gastric ulcer. Few of us realize how recent is the recognition of ulcer of the duodenum. In looking over a succession of old editions of master books such as Osler, Strumpell, and Musser we may see duodenal ulcer emerge rather suddenly about 1911 from autopsy records to a place on clinical charts. Up to this time duodenal ulcer is mentioned by authorities only under the head of "Perforating Ulcer of the Duodenum." This date corresponds accurately with the development of the roentgen examination of the gastrointestinal tract by the bismuth method, which, however, could not have made such headway had it not been supported step by step by surgical exploration. Where this surgical exploration took place is disclosed by Osler, in the edition of 1911 revised by his own hand, in which he says: "From gastralgia, dyspepsia, and hyperchlorhydria, the diagnosis of the chronic, indurated peptic ulcer is very difficult; in many of those conditions, indeed, surgeons have shown clearly that the symptoms are due to an ulcer. That the brothers Mayo should have operated (to June 1, 1908) on 272 cases of duodenal ulcer (as many almost as have been reported in the whole literature) and that Moynihan should have had to June, 1908, 174 cases, indicates that we physicians have been napping, and that what the modern 'gastroenterologist' needs is a prolonged course of study at such surgical clinics as Rochester (Minnesota) or Leeds. It is not as if there were any possibility of mistake, as these are men whose ways and work are known to all. More particularly is the diagnosis of duodenal ulcer important since its relative frequency has been demonstrated." Osler does not mention the roentgen ray but we know that this agent, by a study of living instead of post-mortem pathology, showed that the duodenal bulb, or rather that small extremity of the stomach beyond the pylorus, is the most subject to ulceration of any portion of the alimentary tube from mouth to rectum—and the most nearly immune to cancer. Thus the roentgen ray in a few years, hand-in-hand with surgical exploration, had made greater advances in the diagnosis and treatment of gastric and duodenal ulcer than had been made in all the centuries preceding Roentgen's discovery.

Notwithstanding this extraordinary success, the victory for the roentgen diagnosis of duodenal ulcer seems not to be complete. What about the cases having the syndrome of peptic ulcer, in which the roentgen findings are negative or indecisive? This was the question which Bertrand Sippy put to Carman before the Chicago Medical Society some years ago when Carman reported 98 per cent of accurate diagnoses in duodenal ulcer, proved by operation in the Mayo Clinic. It was a notable occasion where a great clinician met in discussion with a great roentgenologist, the ablest gastroenterologists of their day. We cannot from memory do justice to either; but Sippy's main contention was somewhat as follows: "While it suits the requirements of the surgeon to have indicated, with such remarkable accuracy, the cases in which he will find ulcer, does it meet with the requirements of statistics to thus select only those cases which show unequivocal x-ray signs? What student but could pass his examinations if he could select only those questions which he could answer correctly and conveniently mark off the others? If the roentgenologist diagnosticated gastric ulcer only by the niche-sign he could report also 98 or more per cent of accuracy, but he would be finding only a small per cent of gastric ulcers. Can we ever know the true percentages from operative statistics?"

Carman replied in effect that while he

believed he could exclude duodenal ulcer in most cases with normal bulbs, it was true that there were many indeterminate cases that did not enter into his statistics. With the passing of these two great men, this problem is handed down to the present generation still largely unsolved.

If, as surgeons claim, duodenal ulcer rarely heals spontaneously and usually recurs after medical treatment, then should not post-mortem statistics be close to the truth? Gastric ulcer, we know, will heal under medical treatment. In either duodenum or stomach, scars may mark the site of healed ulcer. Moreover post-mortem statistics include all kinds of cases, not alone ulcer cases. Perhaps internists and pathologists have been somewhat overawed by the brute force of numbers. Ulcer cases running into the thousands make up surgical statistics of unquestionable accuracy and sincerity. Nevertheless, as a diagnostician, knowing our weaknesses, I would hold to post-mortem rather than to surgical statistics.

In the ninth edition of Osler, edited by McCrae, that distinguished pathologist and professor of medicine has added in the first paragraph under the head of "Peptic Ulcer, Gastric and Duodenal," this statement: "Post-mortem statistics show a great preponderance of gastric ulcer but the experience of surgeons has taught us that in a large majority of cases which come to operation the ulcer is outside the pyloric ring." Again, "The surgical statistics have sent our medical figures to the scrap heap." Again, "Of 1699 cases examined post-mortem and collected from hospital statistics by W. H. Welch, 40 per cent were in males and 60 per cent were in females. Surgical statistics show an enormous preponderance of males." Which then are correct, post-mortem or surgical statistics?

When we realize that these cases which surgeons operate upon are the ones very largely in which roentgen examination has given a positive diagnosis of ulcer, then we see that surgical statistics are in part second hand x-ray statistics. Perhaps our roentgenological methods may be re-examined. It is possible that the error is more gastric than duodenal. The symptom-complex of both gastric and duodenal ulcer was thought formerly to be practically the same, and both types of ulcer were treated by most authors under the non-committal head of "Peptic Ulcer." If, in a case under examination, the signs of duodenal ulcer are not present, and if the nichen sign of gastric ulcer is not present, and if no contractures are found, then few roentgenologists have the temerity to make a positive diagnosis that may send the patient to the operating table. Under these circumstances, the majority of gastric ulcers remain unrecognized by the roentgen examination. The Holzknecht sign-complex is rarely ever relied upon since his assistant Haudek discovered the niche. The nichen sign means the penetrating or perforating type of ulcer, and we know these are but a small percentage. Welch records in 793 cases of gastric ulcer examined post mortem, that 288 were on the lesser curvature, 235 on the posterior wall, 69 on the anterior wall, 95 at the pylorus, 50 at the cardia, 29 at the fundus and 27 on the greater curvature. How many of those, on the posterior or anterior wall, could most of us find even by oblique silhouettes or palpation with barium paste? How many at the cardia or in the fundus by any method? Sproull, before this Society, showed that not a single proved case of ulcer has been recorded by the roentgen ray on the greater curvature. Patients may bleed to death from a gastric ulcer so small as to be almost indistinguishable post mortem. It is fair to say that, in the past, roentgenologists have missed many more gastric ulcers than they have found, and that perhaps post-mortem statistics are truer than the statistics that surgeons have been handing back to us as operative findings. Certainly we can look forward with eager interest to the development of roentgenologic methods of delineating the rugae of the stomach which if successful will, we believe, enable us to recognize gastric ulcer as never before, and make

good a reputation that has somewhat outrun our capabilities in the past.

The symptom-complex of duodenal ulcer, once confused with gastric ulcer, has now become fairly fixed and definite because of roentgenologic teachings. If a patient has an epigastric pain coming on from one to three hours after meals, especially in the afternoon; if the pain is relieved temporarily by eating and by soda; if he has an excess of free hydrochloric acid in the gastric juice and at times occult blood in the stools; and if the history shows recurring attacks in the spring and autumn, then the positive clinical diagnosis of duodenal ulcer is more reliable than negative roentgen findings regarding the bulb.

But the clinical background of gastric ulcer will probably always remain complicated and uncertain. The stomach is the field of the symptom-reflex, the land of the clinical mirage. Outside pathology may express itself in terms of stomach symptoms. Dr. William J. Mayo has called the stomach the sign-board of the abdomen on which are written numerous complaints of other organs. Cheney says, no less graphically, that the stomach plays "the part of a radio receiving-set presenting impressions that are produced far away." He, as well as other recent authors, discusses a long list of diseases capable at times of giving stomach symptoms more or less suggestive of ulcer, and in the New Oxford Medicine he devotes a chapter each to Appendix Dyspepsia and Gallbladder Dyspepsia. Negative roentgen findings so far as the stomach is concerned may puzzle and embarrass the roentgenologist. In past sessions, this Society has heard papers on abdominal angina, mucous colitis, the Ménière syndrome, all of which may give stomach symptoms. The Ménière syndrome is striking. Nausea, vomiting, dizziness, ringing in the ears are thought to be unequivocal digestive symptoms; yet we know that the stomach may be normal and the actual pathology causing the symptoms may be found in the internal ear. Other causes of abdominal pain are the crises of the exanthemata, of tabes and of angioneurotic edema.

It is a task for Scotland Yard or a Sherlock Holmes to pick up clues and disentangle the syndrome of intrinsic stomach disease from superimposed reflex symptoms. The original of Sherlock Holmes was, in fact, a physician, a diagnostician who reached conclusions by remarkable observations and more remarkable ratiocinations. As you know, he was a former teacher of Dr. Conan Doyle at the University of Edinburgh. We find his description in the *Atlantic Monthly* of last July: "Joseph Bell, M.D., F.R.C.S., thin, wiry, dark, with a high-nosed acute face, penetrating gray eyes, angular shoulders and a peculiar walk . . . whose trick of diagnosis was a legend of the institution." "He would sit in his receiving room," wrote Doyle the novelist later in life, "with a face like a red Indian and diagnose the people as they came in, before they even opened their mouths. He would tell them their symptoms and even give them details of their past lives, and hardly ever would he make a mistake."

Dr. Harold Emery Jones, a classmate of Conan Doyle, at Edinburgh, records a case with no little dry humor:

"'What is the matter with this man, Sir?' Bell suddenly inquired of a student standing by. 'Come down, sir, and look at him. No, you mustn't touch him. Use your eyes, sir! Use your ears, use your brain, use your bump of perception, use your powers of deduction!'

"The trembling student did his best; 'Hip-joint disease, sir?'

"'Hip, nothing,' retorted Bell, disgustedly. 'The man's limp is not from his hip but from his foot. Were you to observe closely you would note that there are slits—cut by a knife—in those parts of the shoe on which the pressure of the foot is greatest. The man is suffering from corns, gentlemen, and has no hip trouble at all. But he has not come to us to be treated for corns; we are not chiropodists. His trouble is of a more serious nature. This is a case of chronic alcoholism, gentlemen. The rubi-

cund nose, the puffed and bloated face, the blood-shot eyes, the tremulous hands and twitching face-muscles, with the quick pulsating temporal arteries, all combine to show this'—a *symptom-complex*—'But these deductions, gentlemen, must be confirmed by absolute and concrete evidence'—the *pathognomonic sign*—'which in this instance is the neck of a whiskey bottle protruding from the patient's right-hand pocket!'"

THE CHEST

In pre-roentgen days the chest was the exclusive province of the internist. Here he was supreme, the master diagnostician, who touched the highest pinnacle of skill in the art of palpation, percussion and auscultation. Here the laboratory produced its perfect example of fruitful research—the discovery of the tubercle bacillus. The chest was to the medical clinic what the abdomen is to the surgical. Examination of the pulmonary case required time, experience, learning, reasoning and judgment.

What may the shades of Laennec, Skoda, Koch, Trudeau, Osler and a host of departed masters think as they contemplate the handling of pulmonary tuberculosis in certain cities by the Public Health Service even though animated by the best of motives? They would see an ingenious machine operating a roll of emulsion-coated paper like a huge kodak; and roentgen pictures of the chest snapped in rapid succession as a long line of patients file by, one by one. It is a masterpiece of the industrial type of efficiency and the quantity production of machine-made diagnosis. The cost of each case is reduced to a fraction of a dollar, the interpretation of pictures by some one who never sees the patient, not entering into the item of expense. In highly capable hands this work may have its place, if we could overlook the effects of misplaced confidence in negative findings or needless alarm of parents or patients.

But such a state of affairs could never have come to pass if the roentgen examination of the chest had not achieved a truly wonderful success under controlled clinical conditions. The elimination of clinical conditions will be disastrous alike to roentgenologists and patients. Clinicians did not at first yield readily to roentgen claims. Pride of craft was aroused. To rely on roentgen findings was considered a mark of poor training. A vigorous controversy arose which was never settled by argument. As the old masters passed out of active practice, the question seemed to settle itself "as if some silent force of nature had the deciding vote" and we find the clinical masters of today frankly unwilling to give the final opinion until they see the roentgen evidence.

The roentgenologist and the internist are peculiarly alike. Neither is able to distinguish invariably between the tuberculous and the non-tuberculous, to detect infallibly the first signs of incipient disease, or to decide unequivocally between the active and the quiescent lesion. For the recognition of incipient tuberculosis and, in order to distinguish between an active and a quiescent case, why should not the serial plate method be used? It obviously cannot be the rapid serial used in gastric and duodenal roentgenology. As for the length of time required, we must appreciate the fact that the methods of the internist in similar cases are essentially serial. He takes serial temperature and pulse records. He repeats for days, weeks or months his physical examinations. It is only in the well-marked case or in a case where tubercle bacilli can be found in the sputum that he can reach a decision from a single interview. And yet the roentgenologist is expected to reach his decision from a single examination. As well make an instantaneous photograph of an automobile to determine whether or not it is moving as to make a single film of the chest to show whether or not the lesion is progressive.

BONE DISEASE

Bone was the first structure of the body to be demonstrated and studied by the x-ray, yet bone diseases bid fair to be the

last to yield to methods of roentgen diagnosis. The public and the medical profession expect in affections of bones a definite unequivocal diagnosis from plates alone. But in spite of beautiful films with definition and detail that would stand a magnifying lens, we find ourselves too often unable to give anything but an opinion which is nothing more or less than a statement of probabilities. I well remember a section meeting of this Society some years ago when fifty roentgenograms of bone disease from the Mayo Clinic were shown and the diagnosis of each asked from the assembled roentgenologists, who were among the most eminent in America. Opinions included almost every known form of bone disease. Some very definite differentiations were given to prove osteomyelitis, metastatic carcinoma, tuberculosis, syphilis, benign osteitis and so forth. Then we learned that every plate was that of a case of osteosarcoma operated upon and proved by pathological examination. Bone tissue reaction to different bacteria, spirochetes or malignant cells had similar inconstancies that brought confusion. In no other type of diseases are clinical data more important. But even this help is yet insufficient because so much about bone diseases remains unknown.

The sarcoma registry initiated an epoch in the study and understanding of neoplastic diseases of bones and has stimulated research in bone diseases in general. A new precision has been given to the recognition of these lesions by a better understanding of the clinical phenomena. The admirable chart of Geschickter has attempted with considerable success to provide a differentiation of malignant diseases of bone by addition, to the roentgen characteristics, of only two clinical facts, namely, age of the patient and location of the lesion. We may forecast an amplification of this plan whereby roentgenologists will identify bone lesions by methods not dissimilar, though simpler, to those long used by botanists in the identification of plants—where clinical facts along with roentgen factors will replace the characters of flower and leaf.

Clinical facts are multiplying. The influences on calcium metabolism, of the spleen, parathyroids, pituitary, and other glands and organs of internal secretion are being studied. The old riddle of osteitis fibrosa cystica nears solution and pathologic designations may soon supplement such famous names as Paget, Lobstein, Albers-Schönberg, Christian, Schüller, Perthes, Niemann, Pick and Gaucher. But it becomes increasingly clear that the differential roentgen diagnosis of bone disease will always require a correlation with clinical data.

Brilliant examples of x-ray diagnosis from single roentgen characteristics cannot nullify this generalization. The great naturalist Cuvier reconstructed an extinct mammal from a single bone. Paganini is said to have executed an entire musical score on a single string of his violin. Some master roentgenologist may paint the whole clinical picture from a single roentgen finding. But for most of us it will remain forever safer to use the whole clinical picture for the identification of our roentgen findings.

MULTIPLE LESIONS

It is generally assumed that a patient has only one active disease at a time or that by the law of probabilities the simultaneous presence of two symptom-producing diseases in the same patient would be a rare event. Investigation, however, shows that multiple lesions exist in about 50 per cent of cases and that in about 35 per cent unrelated lesions can be found, leaving some 16 per cent of coexisting lesions in chains of cause and effect. Single methods of examination cannot be expected to show these. The combined resources of clinical, laboratory and roentgen methods are necessary. It is obvious that the older the patient and the more chronic the case, the more probable is the existence of multiple lesions. Coexisting multiple diseases in chains of cause and effect are among the

most interesting. Such a chain is seen in gallstones with diabetes. The initial lesion may have been a typhoid fever or some acute disease causing a cholecystitis. Gallstones may follow. As is well known, living typhoid bacilli have been grown from the nuclei of gallstones. From an impacted stone in the common duct, results a temporary occlusion of the pancreatic duct, with the production of a low grade pancreatitis and ultimately a diabetes from a disturbance of the internal secretion of the pancreas, as shown by Opie, of Johns Hopkins, many years ago. Such is the predisposition of the diabetic that pulmonary tuberculosis may supervene, or perhaps a gangrene, or yet a destructive lesion of the phalanges of the big toe. The roentgenologist may find himself in on the case because of the gallstones, or the pulmonary complication, or perhaps because of the necrosis of a bone in one toe. If a diagnosis were attempted without a survey of the case, it is easy to see how defective would be the clinical concept of the case.

Interpretation is the final stage and should be the highest function of the roentgenologist. The foresight of planning and the excellence of technique are all to this end. Some interpretations are accomplished almost wholly by technical means such as the identification and localization of radiopaque foreign bodies and pathologic formations represented by calculi. Stereoscopy alone resolves questions of fractures and dislocations. Other interpretations stop with the recognition of changes and departures from the anatomic or physiologic normal, satisfied with a simple statement as of a pulmonary opacity, an obstruction at the cardia or a filling defect of the stomach silhouette. But a final interpretation is the translation of these changes and departures into terms of pathology and clinical diagnosis. Thus a pulmonary opacity may become abscess or tuberculosis or neoplasm; obstruction at the cardia may become cardiospasm or cancer; a filling defect of the stomach becomes ulcer or syphilis or carcinoma. Here lies the battleground of clinicians and roentgenologists and on the outcome depends largely the professional standing of the roentgenologist. The clinician holds that such interpretations constitute an invasion of the clinical field. It is one of the purposes of this lecture to maintain that the correlation of clinical data with roentgen findings is the legitimate province of clinical roentgenology and constitutes the main reason for the medical education of the roentgenologist. This is why roentgenology is entitled to the recognition of a full professorship co-equal to the chair of medicine or surgery; why entitled to a separate section in the American Medical Association; why investing its followers with all the privileges of professional consultation without discrimination from other specialties. True, there is overlapping of fields, but not more than with medicine and surgery and other specialties without exception.

You will have seen that the practice herein advocated, while exclusively diagnostic, except for roentgen therapy, is not exclusively roentgenological. Far from it. It is this type of practice that may be urged upon the attention of the young graduate contemplating a roentgenological career. Let us call it Clinical Roentgenology. The American Medical Association will not classify us, having no place for a diagnostician. In the American Medical Association List the nearest approach is the internist *or* roentgenologist. To the young roentgenologist after graduation we may say, you are entirely at liberty to undertake any sort of practice which you desire. If you prefer to be a whole-time roentgenologist in a large city hospital, then clinical roentgenology is not for you. Such work is best carried out in cities of moderate size surrounded by many small towns. You can be roentgenologist to a hospital or two without sacrificing your private practice, because in such cities, hospitals are not huge business concerns to absorb general practice and become indifferent to professional considerations. Such hospitals are medical

Frankensteins. Doctors made them and now they pursue their creators like the proverbial monster. Roentgenologists at first begged permission to install apparatus in the hospital basements and have too often remained at the mercy of the institutions.

A private practice is a point of vantage. Professional equality is secured. Unattached patients will come to you for disinterested diagnosis and advice. You will have patients to refer to physician or surgeon for treatment and can give favors as well as receive them. You collect fees instead of a salary. Thus many of the ills which beset modern roentgenology become nonexistent. Full exercise of a medical education increases the interest and satisfaction of your professional life. You can give superior service which is the best basis for competitive effort.

There is an essential difference between cases referred for a definite limited examination—for example, of the lungs—and cases referred on a consultation basis for diagnosis. If you are prepared for consultation work you can furnish a diagnostic survey quite different from the "opinion" of the old-time consultant at the bedside, and quite free from the bogey of negative findings. But the clinical background must be included. A landscape needs the general scene and enough secondary details to give meaning to a stream, a tree or a mountain that has caught the painter's eye. A map needs the surrounding territory through which a road runs, so that the motorist can properly orient himself. The line of the highway on blank paper, however accurate, would not satisfy the traveler. The attending physician needs a diagnostic survey rather than a name for a diagnosis. A specialist may give him a single line on blank paper. But the diagnostic map or clinical picture needs the physiologic and pathologic landscape to give it therapeutic meaning.

Antaeus was invincible so long as he could keep his feet on solid earth. It was only when he lost this contact that Heracles was able to strangle him. The roentgenologist has his struggle with foes, economic and professional, insidious, incessant, indifferent to temporary defeat, that would have him undergo a reincarnation as a technician. But, like Antaeus, he will find himself invincible so long as his feet are planted firmly on the ground of clinical roentgenology.

CALCIFICATION OF THE SUPRARENAL GLANDS IN ADDISON'S DISEASE

ROENTGENOGRAPHIC STUDY

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TUBERCULOSIS of the suprarenal glands has been said, by various observers,[2,6,11] to occur in 69 to 90 per cent of cases of Addison's disease. Although many cases in which there is calcification of the suprarenal gland have been reported, data indicating the incidence of association of these two conditions have not been presented. Roentgenologic evidence of calcification of the suprarenal glands of patients with Addison's disease has been presented in the literature, in the form of isolated reports[4,5,7,8,9,10] of cases, but here again data are not available relative to the frequency of calcification visible in the roentgenograms of such cases, except as considered by the authors in a preliminary report.[1] Because of the absence of such data, this roentgenographic study was undertaken with the objectives of: (1) determining the incidence of calcification in a series of isolated suprarenal glands removed at necropsy in cases of Addison's disease, and (2) determining the incidence of calcification in the suprarenal areas in a consecutive series of cases of Addison's disease.

The suprarenal glands were obtained in 34 cases which had been listed by the pathologists either as Addison's disease or as tuberculosis of the suprarenal glands. A positive clinical diagnosis of Addison's disease had been made in 23 of the cases, and a diagnosis of questionable Addison's disease, in 3 other cases. In the remaining 8 cases there were tuberculous lesions of one type or another. A second group of suprarenal glands, which had been both grossly and histologically adjudged to be normal, was also observed for control purposes.

Both groups were then subjected to roentgenologic examination. Evidence of calcification, or of regions of increased density, were not shown in the normal glands. In the pathologic glands there was wide variation in density, with very obvious calcification in certain cases. The diagnosis of "positive" glands was limited to those in which, in our opinion, it should have been possible to demonstrate the calcification in roentgenograms in life. It is of interest that in several additional glands there were definite, minute, calcified portions which, however, could not, in all probability, have been demonstrated in life. These were recorded as negative.

In the roentgenogram (Fig. 1) of the group of suprarenal glands in which pathologic changes were found at necropsy, three types of calcification were recognized: (1) gross calcification of the entire gland; (2) multiple, discrete areas of calcification throughout the gland, and (3) homogeneous increased density of the whole gland, suggesting a diffuse deposition of lime salts, such as could be expected with a high grade of caseation. The features were confirmed by histologic examination of the tissues, and were further substantiated by chemical evidence of excessive calcium.

Of the cases in which material was obtained at necropsy, there were 23 in which a positive diagnosis of Addison's disease had been made by the clinician. In 6 of these the glands were roentgenographically positive, an incidence of approximately 26 per cent. Of the 3 cases in which the diagnosis of Addison's disease had been given as

questionable, the glands in 2 were positive, and of the remaining group of miscellaneous tuberculous lesions, the glands in 3 were positive. There was a total, then, of 11 cases (32.3 per cent) in the entire group of 34 cases, with roentgenographic evidence of calcification in the suprarenal glands, which it seemed reasonable to assume might have been demonstrated in the living patient if careful studies had been made. Unfortunately, roentgenograms covering the region of the suprarenal glands either had not been taken or were reported negative in examinations made as a routine, and consequently had not been preserved.

The high incidence of calcification demonstrable roentgenographically in the series of isolated glands studied, immediately raised the question of its roentgenologic demonstration in life. A review of the literature revealed that 6 cases have been reported in which shadows in the suprarenal region were demonstrated by roentgenologic examination. Compared with the number of cases of Addison's disease that have been reported, this is a relatively small incidence of calcification as compared with the percentage that might be expected from the results of our previous studies. By taking advantage of modern improvements in roentgen-ray apparatus and in roentgenographic technique, it was thought that it might be possible to show in roentgenograms a higher percentage of calcified suprarenal glands than formerly. Accordingly, in the last several months at The Mayo Clinic, the suprarenal areas have been examined roentgenographically in all cases of Addison's disease.

When roentgenograms of the suprarenal region were made by the ordinary technique by which shadows of both kidneys are projected on the same film, it was found that shadows of calcification in the suprarenal glands were frequently obscured by shadows of vertebrae or ribs. After experimenting with various positions, it was found that an oblique view of the suprarenal region was necessary in order to minimize the superimposition of other shadows. The patient, therefore, is placed supine on the roentgenographic table, and for an exposure of the left gland, the right side is raised to an angle of 30° from the table, and for an exposure of the right

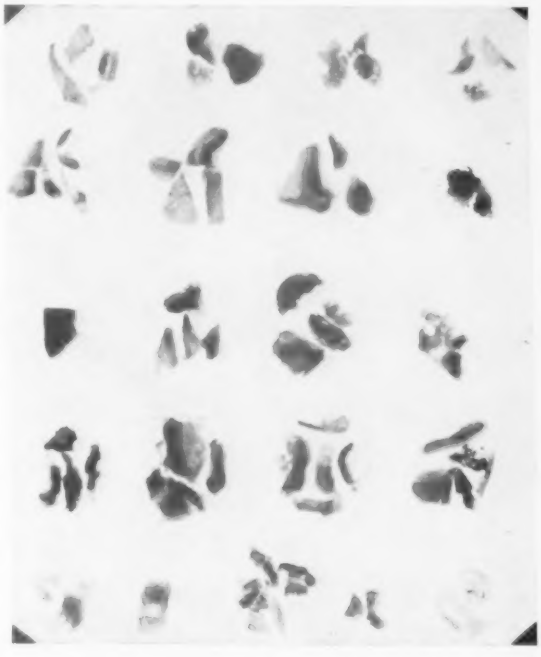
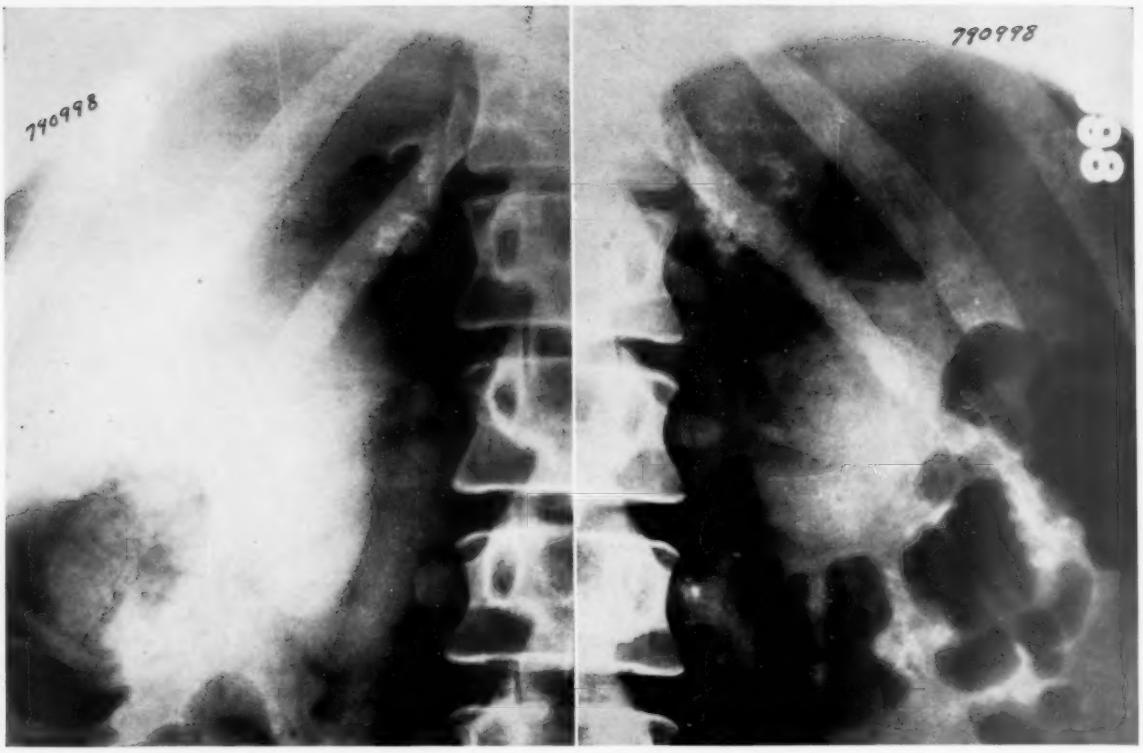


FIG. 1. Roentgenogram of isolated suprarenal glands showing the amount and character of calcification that occurs in the presence of Addison's disease.

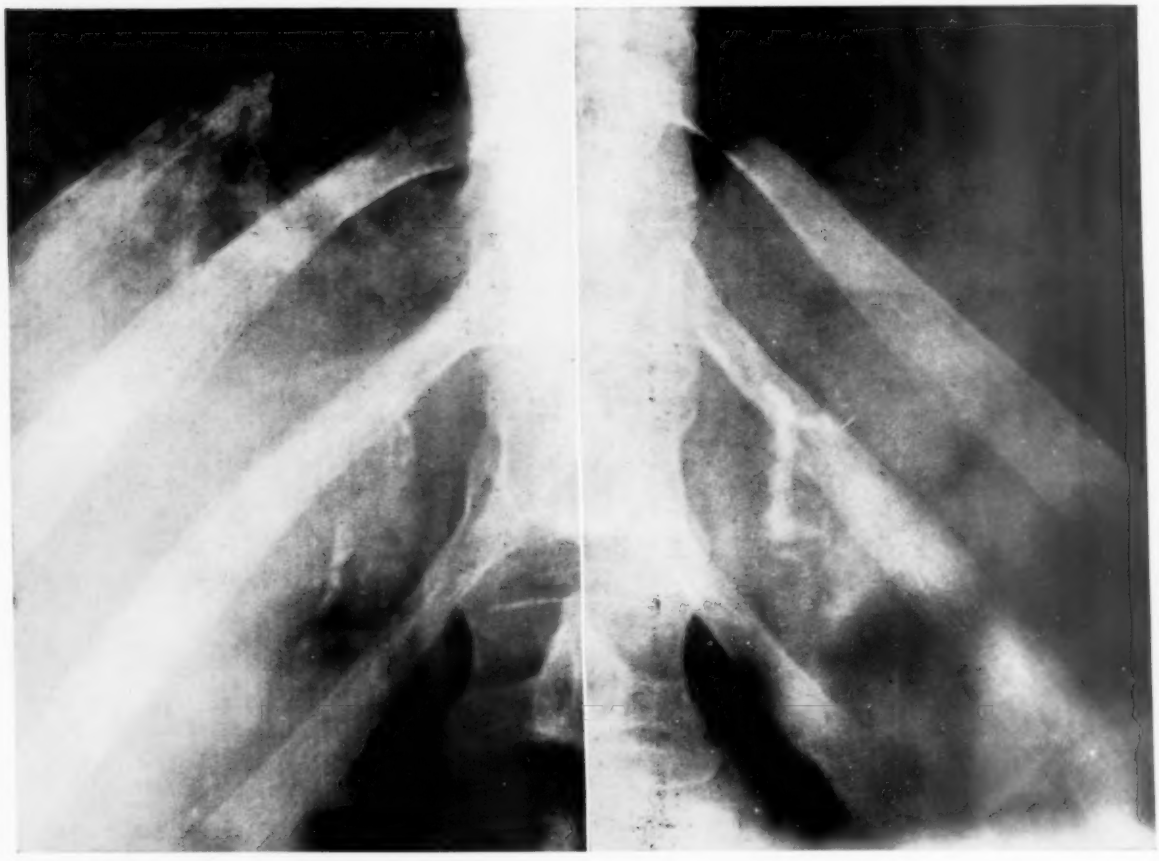
gland, the left side is raised to an angle of 30° from the horizontal. In each case the tube is centered vertically over the tip of the sternum. Stereoscopic films are of considerable assistance.

In the interpretation of shadows of calcification in the region of the suprarenal glands (Figs. 2 and 3), one must distinguish calcification in cartilage of the ribs, calcified mesenteric glands, atypical gallstones, calcified portions and stones in the upper pole of the kidney, calcification in the abdominal aorta and its branches, calcification in a paravertebral abscess, and calcification in an old perinephritic abscess. Since the suprarenal glands move with the kidneys during respiration, films taken at inspiration and expiration will help to identify the shadows of structures that ordinarily do not move with respiration.



a *b*

FIG. 2. *a* and *b*. Calcification of the right and left suprarenal glands in a patient with Addison's disease.



a *b*

FIG. 3. *a* and *b*. Calcification in regions of right and left suprarenal glands in a patient with Addison's disease.

Perirenal insufflation of air, as described by Carelli, should assist in the diagnosis and even permit recognition of normal suprarenal glands, but such a procedure has not been used by us. In questionable cases, correlation of the roentgenographic and clinical data usually will determine the diagnosis. The more chronic pathologic changes, with fibrocaseation or calcification, appear to be most easily demonstrated roentgenologically. In the majority of cases the active disease probably destroys sufficient cortical tissue to cause death before fibrocaseation or calcification occurs. In the cases of Addison's disease due to simple cortical atrophy, the roentgenograms obviously would be negative. From a clinical consideration of the group of cases that is sometimes called "borderline" or "questionable" Addison's disease, positive roentgenographic evidence would be a valuable aid in establishing a diagnosis.

Since using the oblique position for the roentgenologic study of the suprarenal glands, calcification has been observed in 6 of a series of 23 consecutive cases of Addison's disease. This is a much higher incidence than has been previously noted. Although 6 cases are too few from which to draw conclusions, the data certainly suggest that specialized roentgenologic technique is necessary in the study of such cases.

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LEPROSY

A ROENTGENOLOGICAL SURVEY*

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THIS roentgenologic examination on diagnosed leprosy patients at Kalihi Hospital, Territory of Hawaii, was made possible with the consent and approval of Lawrence M. Judd, Governor of the Territory of Hawaii, the cooperation of the Territorial Board of Health, the authorization of the Commanding General of the Hawaiian Department, U. S. Army and the X-Ray Staff of Tripler General Hospital, the Staff of the U. S. Public Health Service Station, Staff and patients, Kalihi Hospital. The work was started in July, 1930 and completed in June, 1931.

In this study over a thousand roentgenograms were taken of the patients in the institution whether or not they showed findings suggesting clinical bone pathology. All hands, feet and chests were roentgenographed (another communication to consider lungs) and sufficient of the skulls, spines, and long bones were included to acquaint us with the frequency with which these bones were affected. Serial roentgenograms, under the same conditions, were done at intervals of about four months on all children under eighteen years of age, as it was soon learned that the hands and feet of this group showed the most rapid and marked roentgen changes. Roentgen examinations were repeated on patients in all age groups who showed marked evidence of disease of the bones or joints. Those who during the ten-month period of study had exacerbations of leprosy with signs or symptoms pointing to a localized involvement of bone were also roentgenographed at short intervals. Certain cases with questionable pathology were followed up by repeated roentgenograms.

The objects of the study were to learn the bones most commonly involved in the disease, the nature of the involvement and, if possible, more definite roentgen evidence of leprosy. It was also desired to know the frequency and time interval with which bone changes occurred and if they had any direct relation to cutaneous and nerve exacerbations.

In our series of 140 cases (ages ranging from six to eighty years; 64 per cent being from sixteen to forty years), 108 were found to have some form of roentgen pathology of the bones, while 32 were apparently normal. Seventy-two, or 50 per cent, showed roentgen changes in the hands and feet. The long bones of the arms and legs showed little evidence of disease. In one case there was a cystic degeneration at the distal end of a fibula, and in another at the end of an ulna, a few other long bones showed periostitis and osteitis associated with leprous infiltration and ulceration of the overlying skin. In 75 roentgenograms of the skull, but one showed bone pathology, namely, destruction in the frontal bone in a case, aged seventeen, with serological syphilis. In a few instances hyperplasia of one or more ribs was seen. The spines were negative except for a small number of deformities and arthritides. Fifty cases were chosen and studied because of the marked soft tissue involvement of the nose and throat, but in no instance was there found roentgen evidence of disease of the nasal bones. This we think is due to the minimal amount of marrow in these flat bones.

The degree of cutaneous leprous involvement is not a reliable index to the amount of bone pathology. Many heavy nodular

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FIG. 1. Case 2936. Note the moth-eaten localized atrophy of the phalanges.

FIG. 2. Case 2875. Note "nick" tip of the right third finger, cystic destruction distal head proximal phalanx, right second finger, and transverse linear condensation of bone heads proximal phalanges, second and fourth left fingers.

FIG. 3A. Case 2714. Patient aged fourteen. Fraying of the tips, distal phalanges, left hand.

FIG. 3B. Case 2714. Note changes in four months, cystic areas of degeneration in phalanges, and head of first left metacarpal.

FIG. 4A. Case 2871. Note "fraying" tip of index finger, and slicing tip of little finger.

FIG. 4B. Case 2871. Six months later, shows recession tip index finger leaving a "nick." Slice tip of little finger.

FIG. 5. Case 2862. Note "nick" and small punched out area near tip, distal phalanx, left thumb.

FIG. 6. Case 2340. Note enlarged nutrient foramina in many middle phalanges. Destructive arthritis and osteitis, fourth and fifth fingers, left hand.

cases in our series showed few or no osseous changes. One of the heaviest nodular cases in the institution showed negligible pathology of the bones (see Case 2744).

The roentgen pathology found was divided for descriptive purposes into:

A. Those alterations of the bones, particularly hands and feet, which showed minute defects such as "nicks," "slices," "frayings," "collar buttoning," grossly prominent or "enlarged nutrient foramina."

B. Grosser lesions of bone, evidencing osteitis, osteomyelitis, cystic degeneration of bone ("leprous osteitis multiplex cystica"). Included in this section are cases which not only show various forms of bone dissolution and destruction, but bone regeneration and construction.

C. Arthritis, destructive and productive.

Thus (A) "nicks" are small defects shown on the films as slits, indentations or excavations of the phalangeal tufts (see Cases 2875, 2871, 2862). A part of the tuft may be diagonally shaved off or "sliced" (Case 3017), the tip of the tuft may be combed out giving it a "frayed" appearance (Cases 2714, 2871, 2973), or the entire tuft may disappear giving the remaining phalanx the appearance of a "collar button" (Cases 3024, 2997). "Enlarged nutrient foramina" are small, round, punched out areas of rarefaction and absorption at the sites of the normal tiny apertures of entrance of nutrient vessels seen commonly near the ends of the phalangeal diaphyses. They are evident rarely in the normal

Fig. 7. Case 2620. Note enlarged nutrient foramina in many middle phalanges, and small cystic area third left proximal phalanx.

hands and feet, but the great and pronounced frequency of this finding in this series (about 30 per cent) leads us to believe that in many cases "enlarged nutrient foramina" are atrophic responses to pathologic leprous vascular supply; the percentage was so high that discernible, prominent, conspicuous, enlarged nutrient foramina, coupled with other destructive bone and arthritic changes, should arouse the possibility of leprosy being at the root of the trouble. (See Cases 2340, 2620, 2973.)

Under (B), 10 per cent of our cases, the films of phalanges, metacarpals or metatarsals show increased radiolucency, honeycombing, spotty osteoporous atrophy, eccentric or concentric atrophy, local, lenticular-like, cystic areas, with peculiar alterations in size or structure; there may be increase or decrease in size of an entire bone; inflammatory cystic swelling of a shaft may appear, leaving both ends of the bone intact. Approximately near the junction of the shafts, with either head, more frequently the distal heads, occurs a dissolution of bone at right angles to the shaft, manifested at first by a "transverse linear atrophy" which later may progress into a complete solution of continuity, a pathological fracture. This specific form of de-

Fig. 8. Case 3017. Note "slicing" tip of left index finger.

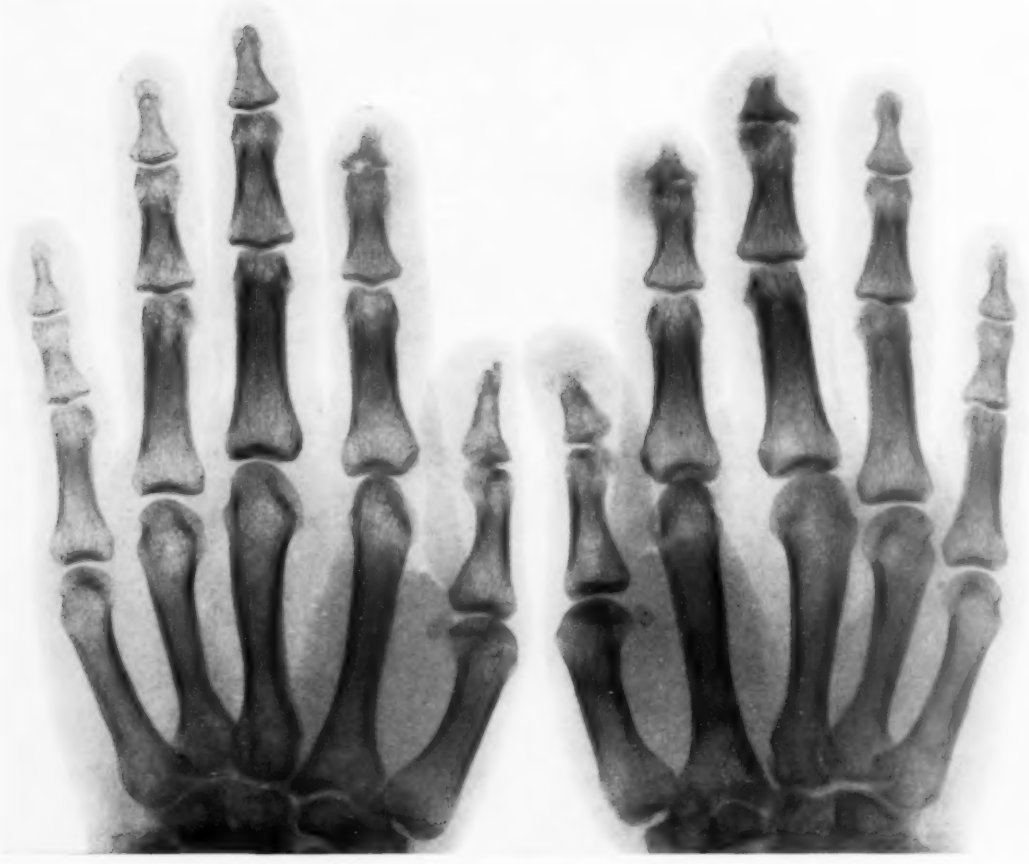

Fig. 9. Case 3024. Note "collar buttoning" three terminal phalanges. Transverse linear atrophy middle phalanges, right second and third fingers. Destructive arthritis. Nutrient foramina accentuated, left fourth and fifth terminal phalanges.

FIG. 10. Case 2973. Note "fraying" right first and second fingers. "Slicing" both middle fingers. "Enlarged foramen" proximal phalanx left thumb.

FIG. 11A. Case 2997. A remarkable osteitis and osteomyelitis of the third right proximal phalanx. Note the swollen and osteoporous diaphysis. Mushrooming head fourth right proximal phalanx.

FIG. 11B. Case 2997. Note changes in five months. Marked improvement in proximal phalanx right middle finger, with union of the epiphysis and diaphysis. Improvement third and fourth terminal phalanges, left. Concomitant destructive osteitis of other phalanges.

FIG. 11C. Case 2997. Taken ten months after Figure 11A. Note concomitant regeneration and degeneration bones of hands.

Fig. 11d. Case 2997. "Fraying" and "collar buttoning" distal phalanges. Destructive osteitis of several phalanges and head of right fifth metatarsal. Destructive arthritis, several interphalangeal joints.

struction might be the result of nerve impairment, pathologic vascular supply or local infection (operating through the nervi nervorum or vasa vasorum, in the capillary beds, or remotely through larger vessels and nerves). We noted it in 10 cases and consider this finding one of the suggestive appearances of bone leprosy. (See Cases 3024, 2498, Fig. 12a, 2787, 2910.)

To comment on the above is to see the wide and extensive variety of bone atrophy, decalcification and demineralization which the films disclose in the bones of the hands and feet of lepers. A generalized homogeneous, diffuse atrophy may be the result of, say, ulnar nerve involvement and be evident in the last two fingers. Localized, multiple, punched out areas of decreased density are significant of osteoporous atrophy. In some instances "enlarged nutrient foramina" could well be pressure or eccentric atrophy from perivascular leprous infiltration; this form of atrophy also results from enlarging lepromata. "Frayings," "nicks," "collar buttoning" emphasize concentric atrophy, though "nicks" might be from perivascular infiltration. "Slices" and "transverse linear atrophy" are the probable result of neurovascular leprous pathology. We believe that some in-

FIG. 11E. Case 2997. Taken five months after Figure 11D. Note concomitant improvement and degeneration.

stances of "transverse linear dissolution" are probably the result of local leprous infection.

This attendant softening and disarrangement of bone calcium from disturbed blood, lymph and nerve supplies to bony centers in young children who have leprosy brings on a sequence of phenomena, prominent among which are pain, inflammatory swelling, with increased local heat and tenderness, exemplified on the film by a mushrooming and telescoping of an articular end of a bone of the hands or feet—an osteochondritis deformans, the result of leprosy, and leaving in the end an arthritis deformans. (See Case 2857, aged sixteen, and possibly 2997.)

Regeneration or healing of the shafts was noted in many of the phalanges but destructive processes in the tufts tended never to heal. Transverse linear areas of dissolution in some instances are replaced by lines of bone condensation. Varying degrees of osteosclerosis replaced areas previously diseased.

The first films on Case 2997 showed a hyperplasia of all parts of the shaft of a phalanx with the exception of the head and the epiphysis, combined with a marked polycystic degeneration. A plate taken five

FIG. 11E. Case 2997. Taken six months after Figure 11D. Note separation of the distal epiphysis, widening of the interphalangeal joint space and fracture of the proximal epiphysis, right great toe. Observe osteoporosis of many of the phalanges.

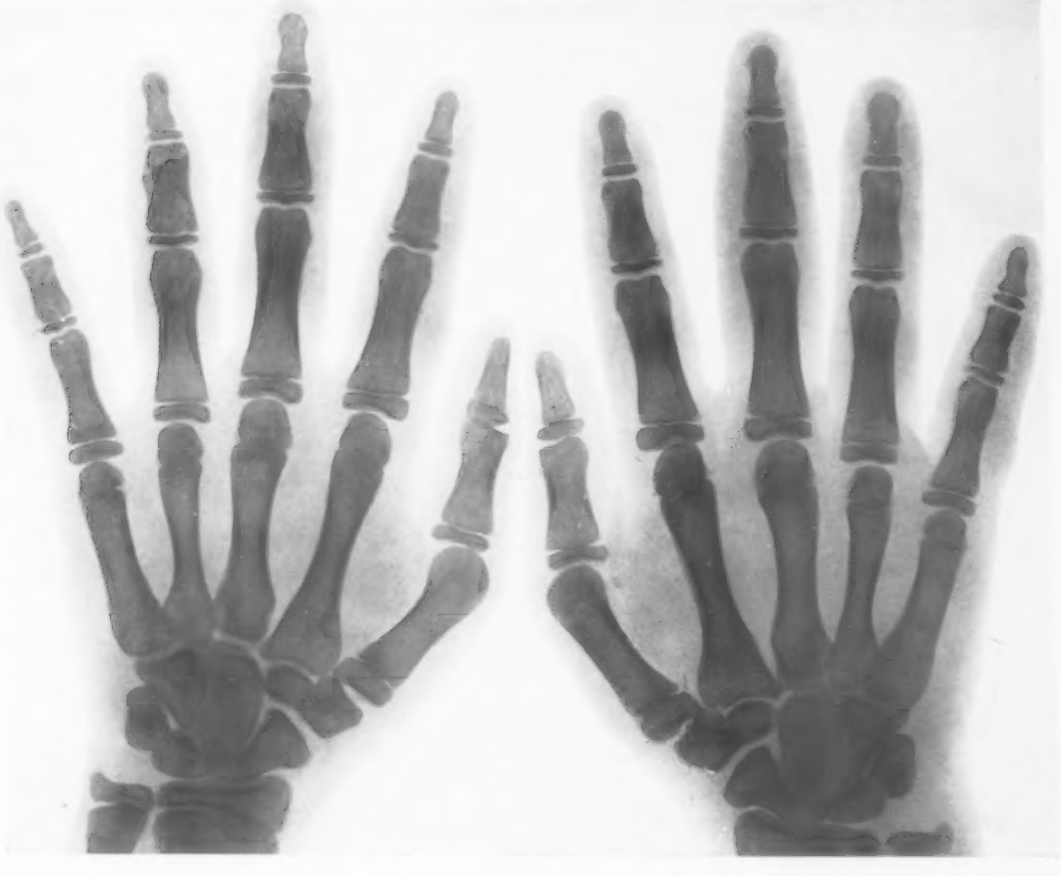

FIG. 12A. Case 2498. Note osteoporosis developing transversely across the bones, near the heads, fifth right proximal, third and fourth and fifth middle, left, phalanges. Destructive osteitis terminal phalanges, fourth and fifth right, third left.

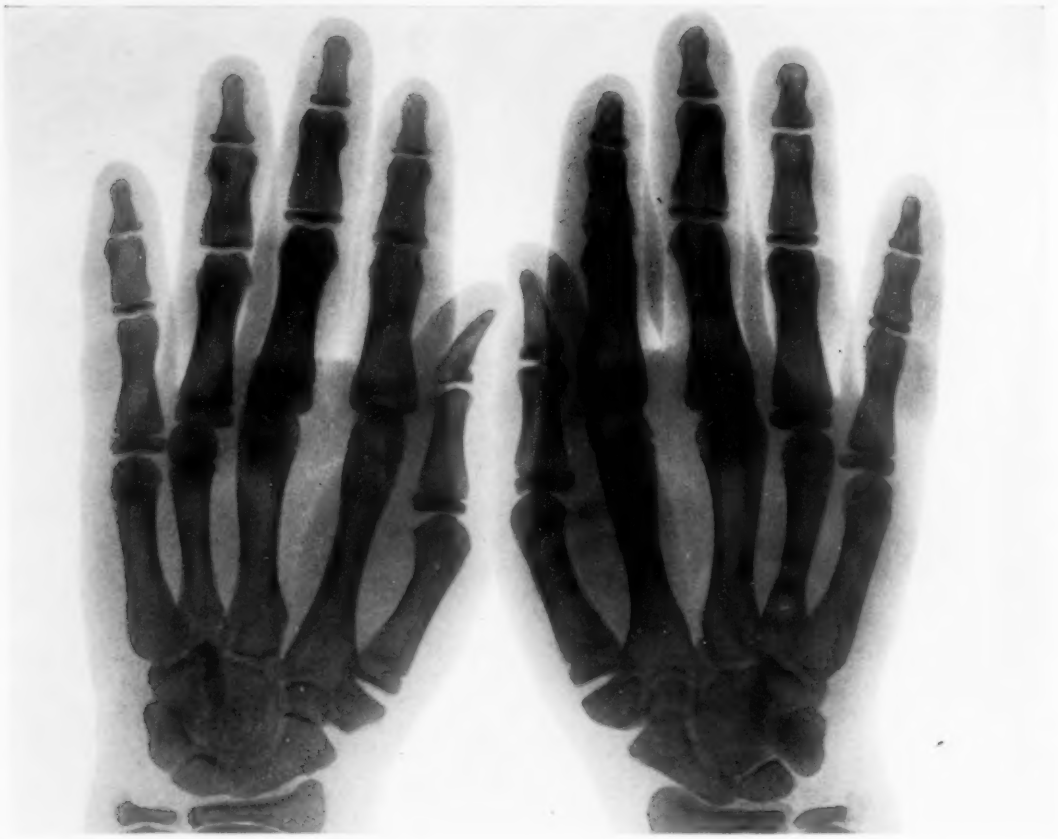

FIG. 12B. Case 2498. Taken nine months after Figure 12A. Note definite improvement in the phalanges, with marked regeneration fourth left middle phalanx.

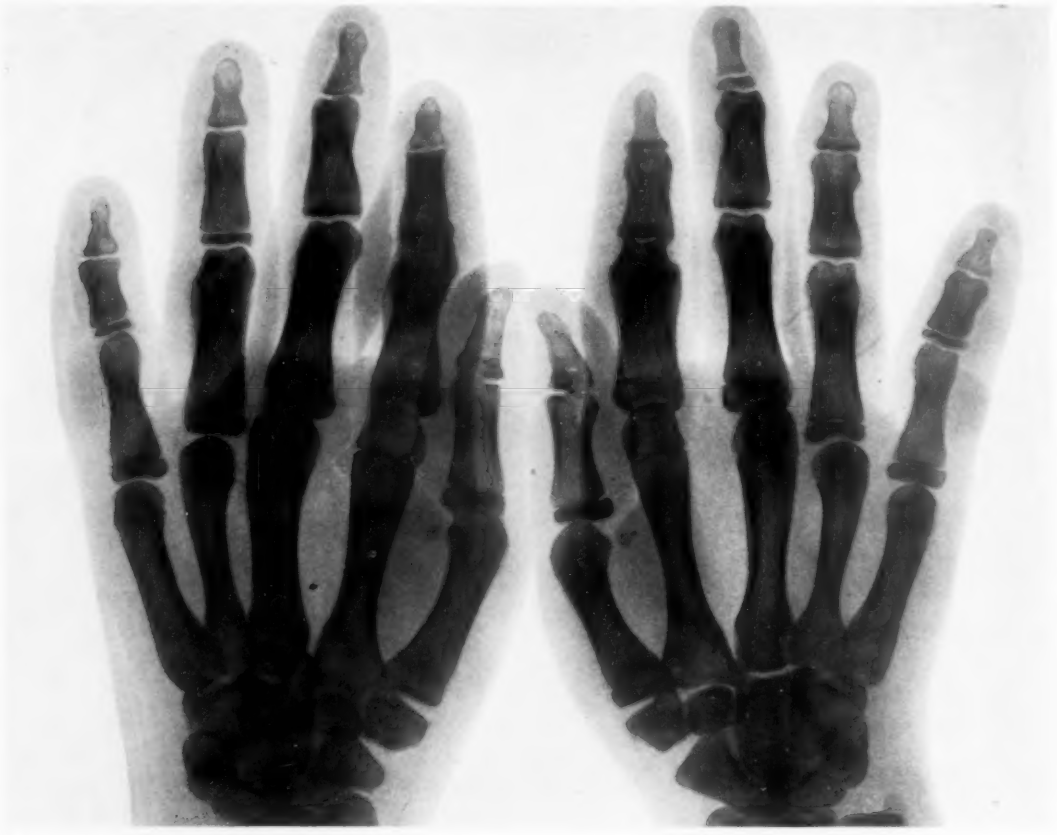

FIG. 12C. Case 2498. Taken four months after Figure 12B. Note retrogression in many phalanges, especially the transverse linear dissolution near heads of the second proximal phalanges.

Fig. 13A. Case 2787. Note absence of marked pathology.

months later showed nearly complete regeneration of the shaft and union of the diaphysis with the epiphysis and a similar regeneration of the third left terminal phalanx. Concomitant with the improvement in two phalanges there was seen extensive degeneration in several other phalanges. A roentgenogram taken of the hands ten months after Figure 11B showed improvement in certain phalanges, accompanied by destruction in others. (See Case 2997, Figs. 11A, 11B and 11C.)

Case 2498 (Figs. 12A and 12B) exemplifies improvement accompanied by the union of the diaphysis with the epiphysis, and also healing in certain phalanges with retrogression in others. Figure 12C shows a secondary degeneration following a primary improvement. These and other cases in the study lead to the belief that the greatest changes in bone leprosy occur during the formative period, that is, at or about the time of union of the integral parts of the bones, and that rapid improvement in one phalanx may be accompanied by destructive changes in others.

It is our belief that in such cases the infection is carried to the bone via the vascu-

Fig. 13b. Case 2787. Taken five months after Figure 13a. Note the transverse linear atrophy near the epiphyses, left second and fifth proximal phalanges.

lar supply and there develops into a subacute leprous osteitis and osteomyelitis. Coincident or subsequent secondary infection via the same channels may play a part in the process.

The infection once localized in a bone may heal with or without the patient's knowledge of its existence, leaving an area of bone condensation, and again it may result in marked destruction with absorption of bone and cystic degeneration.

Case 2924 in three serial roentgenograms showed destructive cystic degeneration probably due to enlarging lepromata. The April figure showed bulging of the shaft. The terminal phalanx of the left finger which went through a similar change was curetted and the material obtained was found teeming with acid fast bacilli.

Case 2864 in three serial roentgenograms showed the development of a cyst-like area. Case 2875 showed beginning cystic degeneration. Another important observation was the finding in several instances of shadows which were interpreted as leprous osseous dactylitis. To this form of bone

Fig. 14. Case 2910. Note transverse linear dissolution near heads proximal and middle phalanges, fifth right finger. Osteoporosis middle phalanx right fifth finger. Beginning linear atrophy, head proximal phalanx, second left. These bones were normal in August, 1930.

leprosy we give the name "osteitis leprosa multiplex cystica," following the same classification as applied by Jüngling[3] to an analogous infection of the bones by *Mycobacterium tuberculosis*.

During the ten months spent in this work 6 patients applied for treatment of acutely swollen painful digits, the skin of which was red and tense and demonstrated an increased temperature locally, with no signs of abrasion or ulceration. Deep pressure over the involved bone caused increased pain and tenderness. The roentgenogram confirmed the diagnosis of leprous osteitis. In these cases it is believed that the disease has been progressing in the bone for some time before the soft tissues become involved and the patient applies for relief. (See Case 2787, Figs. 13A and 13B, and also Case 2910, 2498, Figs. 12A, 12B and 12C.)

In a roentgen study of a rat inoculated intravenously with material of rat leprosy by one of us (J.R.M.), generalized lesions developed in the skin, lung, liver, and spleen. There was also definite roentgen evidence of bone absorption in the distal ends of the radius and ulna bilaterally, and beginning destruction of the maxillary bones. An examination of the bone marrow at these localized areas of absorption showed numerous acid fast organisms, thus

FIG. 15A. Case 2924. Note cystic area of degeneration, proximal phalanx right second finger, probably a leproma, gradually enlarging as demonstrated in the subsequent serial roentgenograms. Similar condition distal phalanx, left fifth finger.

FIG. 15B. Case 2924. Note enlargement of cystic area in five months.

FIG. 15c. Case 2924. Taken ten months after Figure 15A. Note enlargement of the cystic area with bulging of the cortex.

FIG. 16A. Case 2864. Pathological fracture, tip right fourth finger. Beginning destruction, right second terminal phalanx.

FIG. 16B. Case 2864. Taken six months after Figure 16A. Note increased destructive osteitis terminal phalanx, right index finger.

FIG. 16C. Case 2864. Taken one month after Figure 16B. Further absorption in the distal phalanx right index finger. Pathological fracture head, fifth right proximal phalanx. No evidence of bone regeneration.

confirming the diagnosis of leprous osteomyelitis (see Fig. 21). The roentgenograms in this rat were compared with those of ten normal rats.

Arthritis—(27 per cent of our cases). Mechanical arthritides result from the relaxation of tendons and joint capsules due to a primary leprous nerve involvement. Such joints lack the protection afforded by the antagonistic tonus of normal muscles and tendons, and become abnormally mobile so that slight trauma results in destruction of the articulating ends of the bones which would not occur with normal innervation. Following the primary relaxation there is contraction due to destruction of the nerves, giving the more normal antagonistic muscles and tendons control of the member. Many of our patients early in the course of their disease show dorsal flexion of the digits and later the characteristic claw hand. Sensory nerve impairment to pain tends to bone and joint destruction in patients with leprosy due to the fact that injuries are unnoticed until function is disturbed. Fractures unnoticed by the pa-

Fig. 17. Case 2857. Patient, aged sixteen. A remarkable instance of joint destruction. Note hyperplasia middle phalanges of the left hand with mushrooming of the proximal articulating ends.

tients were discovered in serial roentgenograms. Probably there is leprous arthritis, both inflammatory and toxic in nature, and many joint changes in leprous individuals are due to secondary infection by contiguous spread. In the final stage the patients are severely crippled with a deforming arthritis. (Note Cases 2340, 3024, 2857 and 2600.)

DIAGNOSIS

When a roentgenogram reveals a combination or association of shadows indicating involvement of the tufts, shafts and joints of the hands or feet, such as "nicks," "slices," "frayings," "collar-buttoning," "enlarged nutrient foramina," "transverse linear dissolutions" near the proximal or distal extremities with the shafts, worm-eaten, honey-combed appearances of the shafts, leprosy, as a diagnosis, is to be suspected. Further, the roentgenogram discloses that the phenomena in these bones occur in cycles, showing periods of dormancy and reactivation similar to the recessions and exacerbations noted in cutaneous leprosy. These demonstrable alterations in structure are regarded as inflammatory, affecting locally or selectively a bone or bones of the hands or feet. After the initial reaction the bone may regenerate or degenerate. One bone in an extremity may improve at the same time another is retrogressing. This more or less selective, localized sprinkling of pathology in varying stages of degeneration or regeneration is,

FIG. 18. Case 2600. Osteitis, hyperplasia and osteoporosis, middle phalanx, left fourth finger, taken three weeks subsequent to an acute, non-suppurative, inflamed, painful swelling of the finger. Probable leprous osteomyelitis.

from a roentgenographic viewpoint, characteristic of leprosy.

DIFFERENTIAL DIAGNOSIS

Other diseases may show shadows similar to leprosy in the roentgenograms, notably Raynaud's disease, tuberculosis, syphilis, coccidiosis, sceroderma, so-called sarcoid, and other grades of osteomyelitis.

Kornblum[5] states that similar changes occur in Raynaud's disease, and that while leprosy is "from a definite infective agent, its bone changes are not specific." With suspected Raynaud's disease the diagnosis should be in abeyance until leprosy is ruled out. Leprous osteitis and osteomyelitis are specific. Remote nerve and vascular pathology in leprosy would, in our opinion, more clearly simulate Raynaud's disease.

As regards tuberculosis, the caries and necrosis attributable to leprosy on the films is clear cut and sharply demarcated. There is not likely to be "slicing" or "transverse linear atrophy" in tuberculosis. Tu-

Fig. 19. Case 2744. Note absence of marked bone pathology in a very heavy nodular case.

berculous lesions about and near the joints are likely to throw a haze on the films. It might be impossible to differentiate osteitis tuberculosa multiplex cystica from "osteitis leprosa multiplex cystica" roentgenographically.

Doub and Menagh[2] reported 2 cases of sarcoid, which in the discussion was considered to be atypical tuberculosis. Leprosy was not considered in the differential diagnosis, but these cases could well have been leprosy, the result of guinea pig injections from the infective material being negative. Köhler[4] pictures a rare case in which leprosy was not considered, though it could have been the etiologic factor.

Syphilis and coccidioidal granuloma[1] are both likely to show a proliferative periostitis of the hands and feet, which is markedly absent as a whole in leprosy. In addition, these diseases tend to affect grossly other bones than the hands or feet. Coccidiodal granuloma is rapid in onset and development and shows "less atrophy of adjacent bone." Leprosy does not extend into neighboring joints. Sequestra and involucrum formation are not usually observed in uncomplicated leprosy.

FIG. 20. Case 3014. Note periostitis and deformity of the fibula, associated with heavy leprous infiltration of the soft tissues.

CONCLUSIONS

1. Leprous osteitis, osteomyelitis and arthritis occur in the bones and joints of the hands and feet often producing a characteristic appearance in roentgenograms.

2. The bones of the hands and feet of the young growing individual show in the roentgenogram the most interesting and marked developments attendant on leprous infection.

3. Leprous children should have roentgenograms taken of their hands and feet at intervals of three to six months, and the films kept to observe the incidence, variety and evolution of leprosy as it affects the bones of these extremities. It might be possible to register by this means in suitable cases various effects of different forms of treatment.

4. The most marked changes occur at or about the time of the union of the diaphyses with the epiphyses. Startling improvements have been seen in individual bones in which there was a union of the diaphysis with the epiphysis.

5. Degeneration, regeneration, retrogression and improvement take place in the bones of the hands and feet with about the same constancy as seen in cutaneous or nerve leprosy (soft tissue leprosy). These processes may be coincidental.

6. Changes for the better or worse in bones of the hands and feet have herein

FIG. 21. Rat leprosy. Note areas of absorption at the distal ends of the radius and ulna, also maxilla. Necropsy disclosed numerous rat leprosy bacilli in these areas.

Fig. 22. Normal rat.

been depicted, often going on simultaneously in as short an interval as four to six months. In leprous children, where no previous involvement of bone is discernible, destructive changes attendant on leprous infection may be revealed on the films in four months or less.

7. A rather striking similarity is noticed in the young growing bones of the hands and feet, somewhat analogous to that group of juvenile diseases affecting various portions of the skeleton grouped under the category—osteochondritis deformans or osteo-chondro-tropho-dystrophy.

8. Rat leprosy, in the experiment reported, showed a definite leprous septicemia, with roentgenologic and laboratory evidence of the same.

9. A diagnosis of tuberculosis of the bones of the hands and feet should be cautiously made before eliminating leprous osteitis and osteomyelitis as these lesions may easily be confused, and in all likelihood have frequently been misdiagnosed in the past.

10. Similar and prolonged roentgenological surveys elsewhere are indicated.

11. Leprous affection and infection of the bones of the hands and feet reveals a multiform combination of lesions comparable to the many, often dissimilar arrangements of leprous pathology of the skin.

12. Careful evaluation of roentgen findings depicted and enumerated should lead to a suspicion and then a clinching of the diagnosis of leprosy in obscure cases.

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THE OCCURRENCE OF MULTIPLE BONY LESIONS SUGGESTING MYELOMA IN THE SKELETON OF A PRE-COLUMBIAN INDIAN

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THE study of present-day human ailments has an interesting corollary in the study of ancient human remains. This must of necessity be restricted to bones. Frequently evidence is present in them of combined bony and soft tissue changes, which produced characteristic lesions similar in every way to disease entities noted today in roentgenograms and at autopsy. The finding of evidence of a rare bone tumor with extensive involvement of the bony skeleton of a pre-Columbian Indian seemed to us worthy of considerable description. Its almost exact counterpart, from the roentgen standpoint, can be found in the teaching files in practically every large clinic.

The bones described here were found in 1930 while excavating an Indian burial site, in a sand ridge, on the estate of Rodger P. Clark on the south bank of the Susquehanna River about five miles west of Binghamton, New York. Here the skeletons of forty-three individuals, varying in age from infancy to senility, were uncovered. They were accompanied by potsherds, pipes, axes, arrowheads, and other artifacts which aided in the dating of the human remains.

Apart from the interesting pathological material found on the Clark site, this excavation is of great importance archeologically for it is the first site in New York State belonging to the period intervening between the Second Algonquin and the earliest Iroquois periods which has been systematically explored. A very brief summary of the hypothetical Algonquin sequence in New York is now essential in order to orient one's perspective in regard to the various waves of Indian culture in this district and to show how the bones described here were placed in their proper historical period.

The work of Parker, Harrington, Skinner, Ritchie, and others has demonstrated an archaic occupation by Algonquin tribes several thousand years B.C. The original influx, probably from the northwest, brought in long-headed (dolichocephalic), high-vaulted (hypsicephalic), and narrow-nosed (leptorrhine) nomadic people who lacked knowledge of agriculture and the ceramic art. These cultural traits were introduced, together with the grooved axe and polished slate ceremonials, by a broad-headed (brachycephalic) Algonquin offshoot which had been turned northward up the Atlantic littoral after receiving southern increments of blood and culture. These invaders, who were a more robust people, differed also from their Algonquin predecessors in possessing a broad or platyrrhine nose. At Lamoka Lake in Schuyler County, the hostile initial contact of these two groups is graphically portrayed by the extensive vestiges left in a large village site. As the invaders moved northward, however, amalgamation with the older population took place, and in a series of sites in the Finger Lakes region, the skull form is intermediate in type, being moderately long (mesocephalic), with a nasal aperture of moderate breadth (mesorrhine). This composite group left its village and camp sites containing characteristic pottery, stone, and bone artifacts over most of the State and was finally encountered by the Iroquois who, pushing their way up the Ohio River, appeared in the southwest corner of New York State about 800 A.D. This virile people, although physically inferior in size to the Algonquins, readily impressed their

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arts upon them. Although racially absorbed in part, their culture dominated. Out of this contact emerged the Third Algonquin Period, its pottery, arrow points, and other implements reflecting Iroquois mastery.

The Clark site has been assigned on anthropological and cultural evidence to the period of first contact between the Algonquins and the Iroquois. The pottery, always the most reliable criterion, combines the typical Iroquois form with the characteristic Algonquin decorative motive and technique, while the skeletons are divisible into two groups, neither of pure "racial" type.[1] One group is characterized by a dolichocephalic, hypsicephalic skull and a broad nose, the second has a mesocephalic, hypsicephalic skull-form also combined with a broad nasal aperture. Their contemporaneousness is proved by the presence of the same ware in the graves of both. Analysis shows that a blending of the characteristic Iroquois type (dolichocephalic, hypsicephalic, platyrrhine) with a submerged factor (dolichocephalic, chamecephalic, i.e. low-vaulted, platyrrhine), seen in many old Iroquois skulls, would produce the first group (D-O-P) while the dominant Iroquois type (D-H-P) combined with the early Second Period Algonquin form (B-H-P), seen as the intrusive element in the key site at Lamoka Lake, would result in the second group (M-H-P) found on the Clark estate. In all likelihood this cemetery dates from the late ninth century A.D. or about six hundred years before Columbus discovered America.

Pathological lesions attributable to inflammatory diseases (arthritis, osteoperiostitis) were apparent on 15 per cent of the skeletons, 90 per cent exhibited dental afflictions which included caries, alveolar abscesses, alveoloclasia, periodontitis, and proliferative changes. All of these conditions, save the one which we describe, occur with about the same frequency on other Indian skeletons of both pre-Columbian and historic age found in the course of our explorations in many parts of New York State. One skeleton demonstrated a widespread destructive bone disease very suggestive of a bone tumor of the multiple myeloma type. If this is a case of tumor, as we think it is, then so far as can be ascertained, it is the first recorded instance of this disease in a pre-Columbian Indian skeleton.

Fig. 1. The skeleton was found in the grave with thighs and legs flexed. The defects described in the text can be seen in the skull, clavicles and ilium.

The skeleton, that of a senile male, is shown in Figure 1 as it lay in the usual flexed position in a grave dug two feet deep in the sand. This sand was stained with charcoal from a ritualistic funeral fire. A damaged lozenge-shaped arrow point and three cord-marked pottery sherds constituted the only grave objects. This grave was connected by means of a narrow trench with another which contained the disintegrated bones of an adult male, lying over a bed of charcoal. A fine pottery pipe rested on the pelvis of the latter skeleton.

In the first skeleton, the skull, ribs, sternum, vertebrae, pelvis, clavicles, scapulae,

[1] The terminology and method of classification follow Dixon, Holand B. The Racial History of Man. Scribner's, New York, 1932.

Fig. 2. Photograph of the skull showing 11 of the perforations of the calvarium. These holes are characteristic of a destructive pathological lesion and not the erosion due to weather and age or trephine operations.

certain of the long bones, and certain units of the hands and feet displayed striking areas of destruction. From their nature and the excellent state of preservation of the bones, it is evident that these destroyed areas cannot be attributed to post-mortem

Fig. 3. Lateral roentgenogram of the skull showing numerous areas of destruction involving the inner table as well as the whole calvarium. Note the general uniformity of the density of the uninvolved portions of the skull.

Fig. 4. Posteroanterior roentgenogram of the skull showing the multiplicity of the defects in the frontal and parietal regions. The sinuses are well developed. The orbits are almost oval.

changes although the effects of this process are visible on some parts of the skeleton. Figure 2 shows 11 of the 37 perforations of the cranium which vary from a few

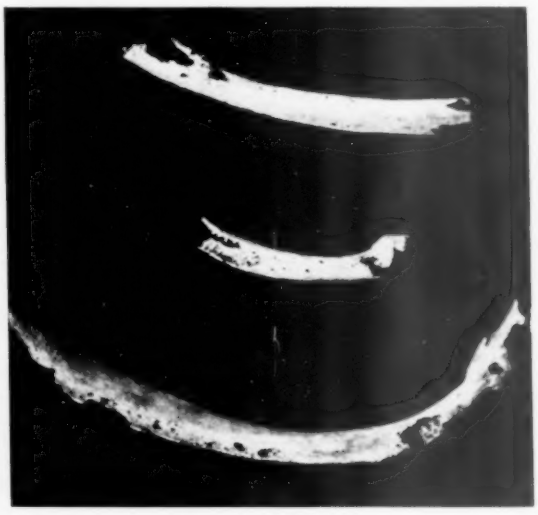

Fig. 5. Photograph of the characteristic expansile lesions in three of the ribs. These could be simulated only by a rapidly growing tumor mass situated in the marrow. Multiple myeloma frequently produces just this change in ribs.

millimeters to 25 mm. in diameter and occur in all parts of the skull. Absorption clearly began in the marrow of the calvarium, for transillumination and the roentgenograms disclose rarefied areas and cavities between the tables of the calvarium. These exhibit a cribriform appearance in many places. The mandible, too, was affected. The right coronoid process fractured at a touch when removed from the ground while the interior of the left ramus was entirely destroyed (Fig. 3).

The extent of the involvement of the ribs, sternum, and vertebrae may be judged from Figures 5 to 9. Several of the former appeared ready to fracture as the result of the expansive and absorptive force applied to their interior. The distended areas seen on two examples which were too fragile to preserve intact are illustrated in Figure 5. In the vertebrae the bodies, arches, and spines are equally affected. The left ilium and scapula, given in Figure 8, are typical of their companion bones. Considerable post-mortem erosion may be seen on the pubis and iliac crest, while the iliac fossa and ischium bear pathologic perforations. The large opening in the left scapula measures 30 mm. in its greatest diameter. Its irregular margin, bordered by numerous perforations, exhibits a lip-like eversion. This is very suggestive of expansile pressure.

Fig. 7. Roentgenogram showing multiple pathological lesions. Several of the ribs show evidence of pathological fracture with callous formation at the site of fracture. Note the thinned cortex in many of the ribs.

Fig. 6. Photograph showing extensive lesions in other bones. The lower edge of the gladiolus shows the effect of erosion as well as the pathological lesion.

But few lesions occur on the long bones, those in evidence being near the extremities. Of the examples given in Figure 8, pathologic destruction of the bone may be seen on the neck of the right femur and along the posterior intertrochanteric line of the left.

Roentgenograms of these bones show a constant type of destructive lesion involving the central or marrow portions of every one of the flat bones and the vertebrae. There are also a few punched out, circumscribed areas on the long bones, namely,

the humeri, clavicles, and femora. The tibiae, radii, ulnae, and long bones of the hands and feet are not involved. These destructive lesions are either circumscribed and roughly spherical or irregular, ragged, and confluent. The cortex nearby is thin and sharply outlined and, in the ribs, often bulged or flaring where the bone has been broken off through such an area. Evidence of callous formation around pathological fractures through such areas in the ribs is numerous.

Fig. 8. Photograph of the left scapula and left ilium and the femora showing the more extensive involvement of the flat bones. The left ilium shows relatively little erosion, most of the destruction being due to the pathological process.

In roentgenograms of the pelvic bones, the sacrum, and several of the vertebral bodies, roughly spherical, rather sharply outlined masses of very dense material, almost suggesting eburnated bone, are apparent. There are collections of these in the lower portions of the ilium, which are almost symmetrically shaped and the largest of any of these masses. The destructive process usually involves the areas surrounding these dense masses or contiguous areas.

The only other abnormalities are changes chiefly relating to the bodies of the vertebrae. There is some flattening and atrophy of the surfaces in the region of the intervertebral discs, and hypertrophic spurs and lipping are present on the edges of most of the lower vertebrae. These changes are consistent with a degenerative arthritis having bony proliferation. Most of the teeth of this skull have been lost. Those which remain are small and dense, showing some retraction of the alveolar border suggesting alveoloclasia. There is, of course, a great deal of atrophy of the jaw bones where teeth are missing. The head of one humerus is rather flattened and atrophic. This may in part be due to a partial collapse of the head of the femur from involvement of the upper portion by the destructive process, or it may have been due to a change in posture since the shaft, just below the lesser trochanter, is somewhat thickened and irregular, suggesting an old healed fracture in this region. The changes in the femur have caused a realinement of the lines of force in the acetabulum and ilium so that they are not symmetrical on both sides.

The location and multiplicity of the bone lesions suggest a pathological process with multiple foci of almost simultaneous origin in the marrow portions of all of the flat bones. The character of the destruction and the evidence of expansile bulging and lipping of some of the lesions in the ribs suggests a rapidly growing tumor process rather than an inflammatory process. Since the skeleton is that of a male, a breast tumor can practically be ruled out. Hypernephroma, if disseminated to this degree, would probably involve the long bones as much as the rest since its metastases would be blood borne and its lesions would be more circumscribed. It would produce the expanded areas but would be less likely to have as many ragged irregular lesions.

Carcinoma of the prostate of the destruc-

tive type could simulate these changes, especially since it involves the medullary portions of the bones. Prostate tumors do not, however, involve the flat bones so diffusely. They usually restrict themselves to the pelvis and vertebrae though, of course, an extensive, destructive lesion of the type noted here could be produced by the more rapidly growing prostate tumors. Often with prostate tumors there is a combination of destruction and of proliferation. The latter is apt to be diffuse and does not produce discrete spherical masses such as those noted in these remains.

The question always arises in the discussion of early human remains as to whether or not syphilis is present. In these remains, the purely destructive character of the lesion in the absence of proliferative changes would rule out syphilis entirely. The dense areas described in these bones do not conform to any of the usual syphilitic proliferative bone changes.

The lesion known as multiple myeloma is thought to have multiple foci of orgin in the bone marrow. It forms masses which cause erosion and expansion of the bone. Every pathological lesion in these skeletal remains can be simulated by multiple myeloma except the dense hard masses in the various bones. These we have neither seen in multiple myeloma nor can we find such masses described. These dense masses resemble occasional stony, hard masses of

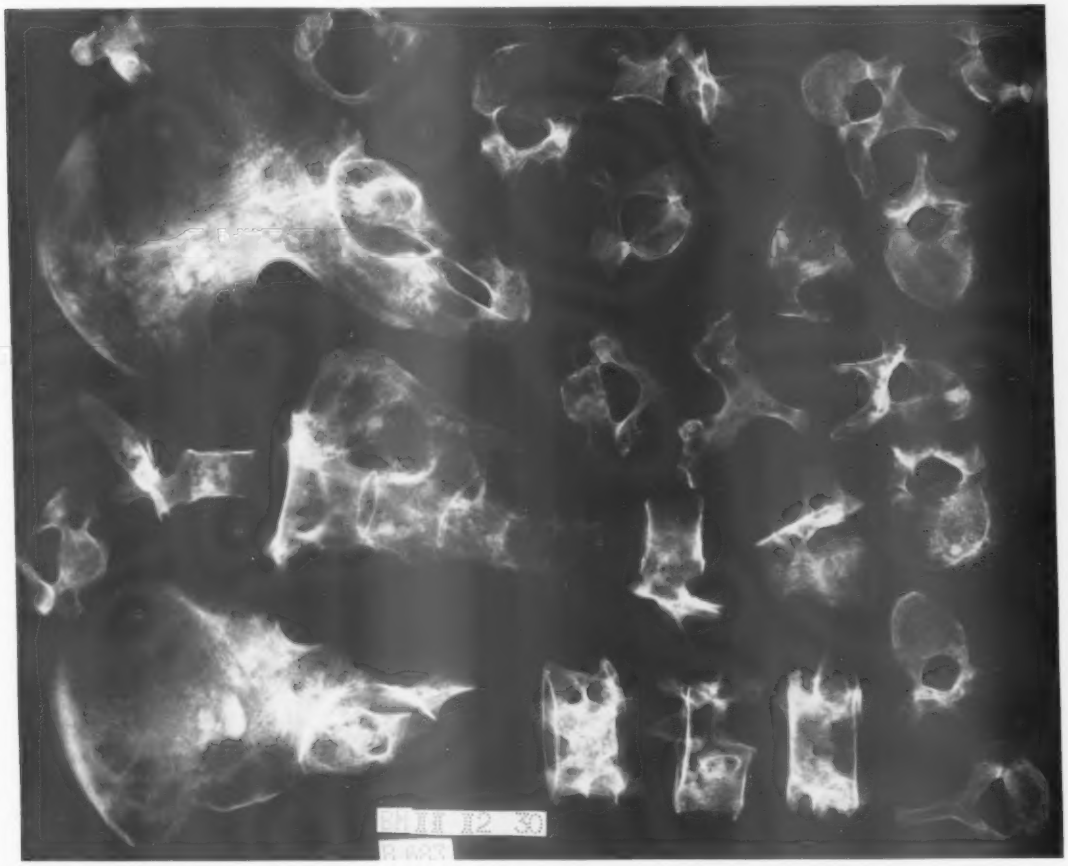

Fig. 9. A roentgenogram showing the small, very dense masses within areas of destruction in the ilia and several vertebral bodies. The symmetrical distribution of these bodies in the ilia would suggest that they were not related to the destructive process.

bone of unknown etiology in normal adults, but the number in this skeleton is rather too great to include them under some other etiology than that having to do with the generalized destructive process.

After a great deal of discussion among our own group and personal communication with Dr. Herbert U. Williams of the Buffalo Medical School and Dr. Roy M. Moodie, paleopathologist of Santa Monica, California, we have come to the conclusion that this must be a case of multiple myeloma since this pathological entity would explain so many of the lesions.

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UMBRATHOR IN UROGRAPHY

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SINCE the inception of urographic diagnostic methods, the question of a choice of contrast medium has occupied the attention of the investigators in this field. Many types of solution, both electrolyte and colloid, have been tried and found wanting in one respect or another.

In this presentation, we are reporting the use of umbrathor in urography.

The first roentgenograms of the urinary tract were made by James McIntyre, a Scotch surgeon, who in 1896 detected a renal calculus by this means.

In 1904, Klose[7] used a bismuth suspension for pyelographic study but found that particles of bismuth adhered to the renal pelvis and ureter, these acting as foreign bodies.

In 1906, Voelcher and Lichtenberg[11] in Germany were the first to demonstrate the complete outline of the ureter and renal pelvis in roentgenograms. These workers used a colloidal silver called collargol. In attempting to outline the bladder, it was discovered in one of the roentgenograms that the solution had entered the ureter and renal pelvis and that they were outlined as well. Lichtenberg was the first subject upon whom collargol was used for pyelographic study. The toxicity of collargol, however, soon caused it to fall into disrepute.

In 1913, Kelly and Lewis[6] used silver iodide, which was discarded.

In 1915, Burns[3] used a neutral solution of thorium nitrate and sodium nitrate. It was the first electrolyte. It was discarded due to its irritating properties.

In 1918, Cameron and Grandy[4] used a 25 per cent potassium iodide and sodium iodide. They later suggested 13.5 per cent sodium iodide.

Weld[14] in 1918 suggested the use of sodium bromide 25 per cent.

Sodium bromide, potassium and sodium iodide and thorium nitrate are not retained in the kidney pelvis more than one and one-half hours when the ureter is ligated, but are absorbed rapidly, apparently from the medullary portion of the kidney.[15] Sodium bromide is more irritating to the mucous membranes than either sodium iodide or thorium.

The solutions of halogen salts are of sufficient molecular weight to cast good roentgen shadows and due to their apparent safety are universally employed in urography.

Finally, a 12 per cent solution of sodium iodide was selected because of its molecular weight, together with the selective absorptive property of iodine, at the same time giving a highly satisfactory opacity to roentgen rays.

In 1921 Stern and Ritter[10] reported the use of an intravenous solution of sodium iodide which was a 10 per cent solution.

In 1921 Clarence Bandler strongly advocated sodium iodide 12.5 per cent in specially devised sterile ampules colored with indigo carmine which is used routinely to date.

Roseno,[9] in 1929, using a substance which combined iodine and urea, obtained good roentgenograms, but unfortunately the substance was toxic to some patients and consequently did not meet with general acceptance.

Von Lichtenberg and Swick[12] in 1929 brought forward uroselectan (42 per cent iodine) which is used chiefly intravenously.

Bronner, Hecht and Schüller[2] introduced abrodil (called skiodan in America) which is a 52 per cent iodine organic compound and is now used universally.

Von Zeissel of Vienna, in 1902, worked on cadavers to study cystograms.

In 1904, Kellan did air cystograms.

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In 1921, two German roentgenologists, Baensch and Boeminghaus,[1] employed vesical examination in the lateral position after injection of a 10 per cent solution of sodium iodide.

Suspensions of bismuth subnitrate and barium sulphate have been utilized by European workers, notably Papin, Gangeleu and Uray.

Iodized oil, particularly lipiodol, advocated by Sicard and Forestier, has gained popularity.

Pfahler[8] in 1919 reviewed his experience with pneumocystoroentgenography in diagnosis of neoplasms of the bladder.

An ideal contrast medium for retrograde pyelography must be composed of material inert and non-toxic. It should have a high value as contrast medium, be non-irritating to tissue and membrane, of low osmotic pressure, and be entirely eliminated within a reasonable time. Furthermore, the solution, if injected intravenously, should cause no ill effects.

In the search for a colloidal medium that would not present the disadvantages of the bromine and iodine compounds, nor the poisonous activity of silver preparations, a thorium dioxide solution was developed, which by the addition of an inactive protective colloid was made miscible with body fluids without being precipitated or otherwise affected.

For cystographic study a non-irritating, non-toxic and inexpensive solution is advisable.

Umbrathor is a 25 per cent thorium dioxide solution, a stable brownish liquid, transparent in transmitted light and of milky appearance in reflected light. If the product is stored over a long period of time, a small amount of sediment may appear, which is, however, not objectionable, and is redissolved upon shaking the bottle. Umbrathor is non-toxic and is not absorbed. It is well suited for photography of the bladder. When it comes in contact with normal mucosal surfaces, it is flocculated thereon as a surface coating, and is thus used in the production of relief pictures. Several European workers[5,13] have arrived at similar conclusions.

Mode of Administration.

1. Have the patient void.
2. Roentgenograph the entire urologic tract.
3. Catheterize the patient and estimate the residual urine.
4. Distend the bladder with boric acid solution, estimating the bladder capacity.
5. Empty the bladder and then inject an equal amount of umbrathor diluted with equal parts of water. This does not decrease its efficiency as a contrast medium. About 50 c.c. umbrathor is usually used. The distribution of umbrathor in the urinary bladder is accomplished in five to ten minutes.
6. The umbrathor solution is then drained from the bladder and about 30 c.c. less air is injected than the bladder capacity. The roentgen exposures are carried out at once to make certain that the mucosal coating of flocculated umbrathor is intact. If the exposure is delayed too long after the umbrathor is drained, part of the flocculent coating may separate.

REPORT OF CASES

To demonstrate the use and abuse of umbrathor, we present 4 cases:

CASE I. Mr. F., aged sixty, reported with a history of hematuria, nocturnal and diurnal frequency.

Cystoscopic examination revealed a tumor mass located in the left lateral wall of the bladder. Due to the position of the growth, it was difficult to note the extent of the neoplasm. Therefore, it seemed advisable to study the patient with the technique described above.

The cystogram (Fig. 1) obtained from the combined umbrathor-air filling showed the tumor definitely outlined. It appeared to be in a resectable portion of the bladder and suitable for surgical intervention. Findings were confirmed at operation.

CASE II. Mr. H., aged seventy, reported complaining of nocturnal and diurnal frequency, together with hematuria, for a period of over two years. Two years before he had been oper-

ated upon, a suprapubic prostatectomy having been performed.

Cystoscopic examination revealed a small papillomatous mass located behind the trigone which was definitely elevated.

Due to active bleeding and the suspicion of a diverticulum, we employed umbrathor-air filling for cystography to aid in outlining this mass.

The roentgenogram (Fig. 2) demonstrates a small irregular filling defect which appears close to the sphincter because of angle of exposure; but it is, in fact, behind the trigone.

Fig. 1.

This being a small mass, surgery was suggested and carried out. A definite tumor within a diverticulum was found. Diverticulum and tumor were removed. The patient made an uneventful recovery.

Case iii. Mr. W., aged forty-five.

In our extreme desire to note the value of umbrathor in studying the seminal vesicles, a vesiculogram was done in a case of sterility. The seminal vesicles, vas deferens, and epididymis are well outlined, as is seen in Figure 3. However, this drug remained in the seminal vesicles for many weeks and we feel that this was due to a possible obstruction, the umbrathor acting as a foreign body, and it therefore should not be used in vesiculography.

Fig. 2

Case iv. Mrs. P.

Due to excellent cystographic studies obtained, we used a solution of umbrathor for pyelographic study. The roentgenogram, as seen in Figure 4A, shows a well-defined renal pelvis and ureter from which a reading is readily made.

Fig. 3.

However, the same evening following this procedure, the patient had severe chills and fever, with acute renal and ureteral colic and anuria. It was necessary to hospitalize this patient and administer large doses of morphine for the relief of pain. She remained in the hospital for ten days before returning to normal.

Figure 4B, taken one week later, shows some of the solution in the renal pelvis, and the lower ureter still completely filled.

This demonstrates the dangers of umbrathor in pyelographic study and here too it should never be employed.

Indications. The use of umbrathor in urography should be limited to the study of the urinary bladder.

Contraindications. Umbrathor should not be used for the demonstration of the seminal vesicles. It is absolutely contraindicated in pyelographic study. Where a suspicion of a vesicorenal reflux exists this procedure should be practised with a great deal of caution.

CONCLUSIONS

1. Cystographic examination of the bladder is of great value in establishing the existence of vesical neoplasms, prostatic obstruction, or diverticula. It is of particular value in complete examination of the bladder in cases of obstruction of the urethra, excessive hematuria or intolerance on the part of the patient to instrumentation.

FIG. 4A.

FIG. 4B.

2. The existence of a neoplastic growth in the bladder is indicated by a radiopaque shadow cast by the deposit of the umbrathor.

3. The umbrathor-air filling shows a very distinct relief picture wherein the borders of the tumor are very clearly differentiated.

4. It aids materially in determining the extent of the tumor.

5. It aids in determining the procedure, whether palliative or radical, to be used in the treatment of various cases.

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DIAPHRAGMATIC HERNIA IN A CHILD

REPORT OF A CASE

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THE diagnosis of herniation of the diaphragm is often difficult without the aid of roentgenological examination. It is still more difficult if the patient is symptom-free and if there are no signs that suggest any abnormality in the chest or the abdomen.

It is not our purpose to discuss here the etiological factors that enter into the formation of diaphragmatic hernias, be they congenital or traumatic. The difficulties in diagnosing the condition have prompted us to report the following case.

CASE REPORT

W.M.H., a colored girl, aged six, was admitted to the William H. Maybury Sanatorium with a provisional diagnosis of pleurisy with effusion in the left chest. The history as given by the mother was entirely negative so far as the child's present illness was concerned, except for frequent colds and sore throat at intervals for a year previous to admission. There was no history of dyspnea, cyanosis, or other cardiac symptoms, cough, vomiting, or discomfort in the chest at any time. There were no symptoms referable to the gastrointestinal tract.

In the past history there was nothing of significance. The child was born normally, showed no signs of abnormality in the chest or abdomen at birth or later. At the age of three she developed measles from which she recovered without complications. She had had no trauma to the chest or abdomen and no other illnesses. There is no record of any symptoms of diphtheria which might possibly lead to paralysis of the diaphragm. The most important thing in the history was the fact that the child was exposed to a tuberculous aunt who lived in the same house with her for several months.

The physical examination on admission showed a somewhat undernourished colored girl, not acutely ill, with temperature, pulse and respirations within normal limits. She was 15 per cent underweight. The eyes, ears, nose and throat were essentially negative. A few very firm glands were palpable in the neck.

The chest was somewhat asymmetrical with very slight but distinct bulging over the precordium. Expansion was unequal with lessened excursion on the left.

Right lung: There were no abnormal or pathological signs elicited by percussion or auscultation.

Left lung: There was comparative impairment of resonance in the apex, axilla and lower third posteriorly. In these areas there were diminished breath sounds on quiet breathing and diminution in the intensity of whispered voice; no râles or friction rub were heard and there were no signs of fluid at the base.

Heart: There was a distinct precordial bulge noticeable particularly in recumbency. The apex beat was slightly displaced toward the mid-sternal line. There was no arrhythmia and there were no murmurs.

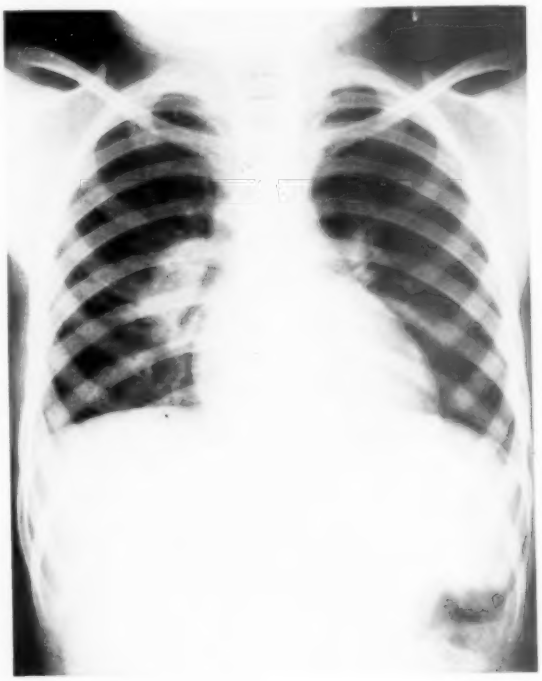

FIG. 1. Roentgenogram of the chest taken six months previous to admission, showing both diaphragms in apparently normal position and shape.

Abdomen: Negative to inspection and palpation. Extremities and reflexes, normal.

Laboratory examinations were all normal. The tuberculin test was positive to 1/1000 mg. of old tuberculin. Admission roentgenogram of the chest (Fig. 2) was interpreted as "childhood type tuberculosis" of the left tracheo-bronchial lymph nodes, and pleurisy with effusion at the left base.

Depending on the roentgen appearance, the tuberculin test and the history of close contact with an open case of tuberculosis, a diagnosis of pleurisy with effusion and tuberculous tracheobronchial adenitis was made, and the patient was put to bed. One unsuccessful attempt was made to aspirate what was thought to be fluid in the chest. At no time did the patient have any symptoms.

At the time of routine check-up examination, the roentgenogram presented an entirely new picture (Fig. 3). The peculiar shadows seen in Figure 3 suggested the possibility of a spontaneous pneumothorax with bands of adhesions between the collapsed lung and the thoracic wall. As there was no history of sudden pain in the chest, dyspnea or any other symptoms that accompany sudden collapse of the lung, we were somewhat doubtful of the presence of air in the pleural cavity; however, a needle was inserted into the pleural space. It was found that the pressure was highly negative and that no air was present. At this time about 100 c.c. of air was introduced into the pleural space under negative pressure. The introduction of the air changed the picture completely, as may be seen by reference to Figure 4. All the "adhesion-like" bands had disappeared, and the only prominent feature of the picture was a high, perfectly smooth and rounded diaphragm with a large amount of gas in the stomach. The lung had collapsed about 25 per cent. This interesting film suggested to us an abnormality of the diaphragm which possibly allowed the stomach to migrate into the left chest. This supposition was easily proved by means of a barium meal which located the position of the stomach and the intestines. In Figures 5 and 6 the extreme degree of herniation may be

Fig. 2. Film taken at the time of admission to the sanatorium. It shows enlarged hilar glands on the left and a shadow resembling pleurisy with effusion obliterating the left costophrenic angle.

Fig. 3. Film taken at time of check-up examination, showing peculiar configuration of the left hemithorax, with "adhesion-like" bands stretching in various directions, giving the impression of pneumothorax. Heart and mediastinum are displaced to the right.

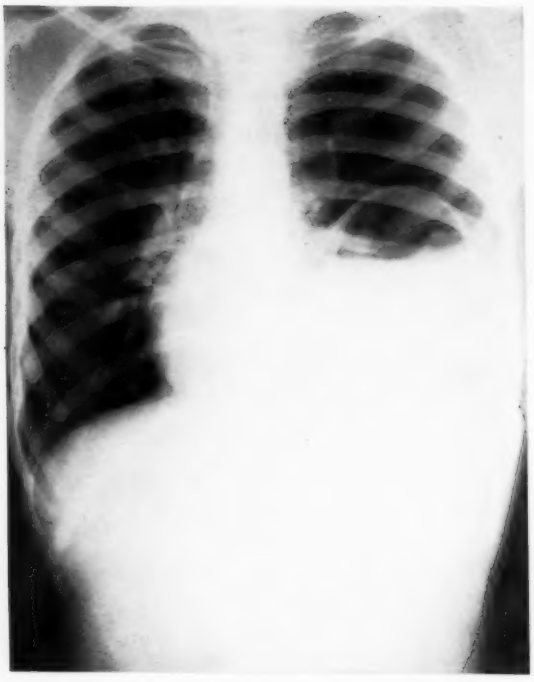

FIG. 4. This film shows the effect of the introduction of 100 c.c of air into the pleural cavity. The diaphragm has resumed its normal shape, although it is much higher than normal with a large amount of gas in stomach.

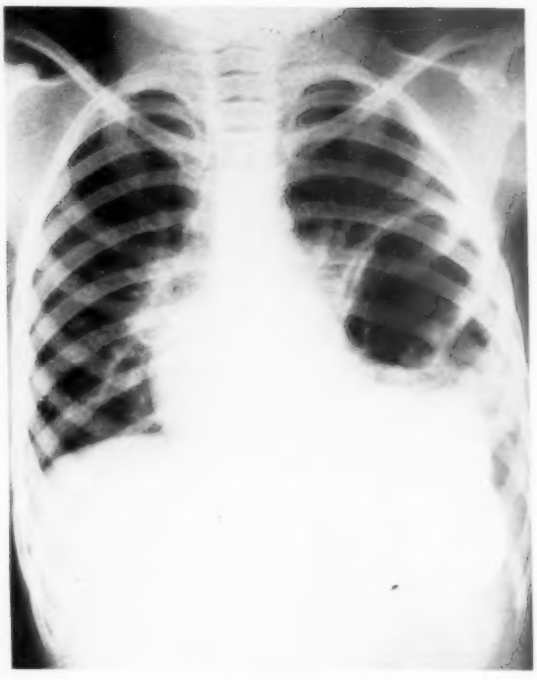

FIG. 5. Film taken immediately after barium meal with patient standing. The herniation is not very conspicuous in this picture.

readily seen. In these films the stomach is seen to occupy almost the entire left chest, carrying with it part of the intestines, and causing marked shifting of the mediastinal structures and of the heart to the right chest.

The provisional diagnosis of pleurisy with effusion made on admission was promptly abandoned and a final diagnosis of left diaphragmatic hernia was made.

DISCUSSION

A diaphragmatic hernia in a child is still somewhat of a curiosity. The case just described is interesting for three reasons: (1) The etiological factor is obscure in that there is no history of any trauma to the chest or the abdomen and no history of previous infectious disease. (2) The condition was not congenital, at least a roentgenogram taken six months previous to admission revealed a diaphragm with an entirely normal appearance. (This film is shown in Fig. 1.) (3) There were no symptoms and no complaints of any sort.

The likely causes of such an herniation may be three, namely: (1) An actual dissection of the diaphragmatic muscle from its posterior attachment, with a peeling away of the parietal pleura by the herniated structures; (2) a rupture of the diaphragm near the posterior attachment, and (3) a weak, undeveloped diaphragmatic muscle which might stretch sufficiently to allow the ascent of the abdominal viscera but which would continue to keep separate the abdominal and thoracic viscera. The first is unlikely because of the probable need of considerably more pressure than could reasonably be conceived of as being present. The second seems improbable because the induction of a small pneumothorax restored the abdominal organs to their normal position without the passage of demonstrable air to the abdominal cavity. The third possibility seems the most likely because of the fact that the herniation was more

Fig. 6. This film was taken with patient in recumbent position, showing the extreme herniation of the stomach and intestines into the left chest with great displacement of mediastinum and the heart.

Fig. 7. Lateral view of the chest showing the relative position of the stomach in the chest.

marked in the recumbent position than when the child was standing. This change in the size and position of the hernia depending upon the posture of the patient was the main reason why the diagnosis could not be made at the time of admission.

As to symptomatology, it is very surprising not to find in this child any of the classical symptoms and signs of an extensive hernia of the diaphragm. During her stay in the sanatorium, she was perfectly well and very active; she experienced no dyspnea, cyanosis or cough, neither on exertion nor on lying in bed with a full stomach. The severe shifting of the heart and the mediastinum caused her no discomfort, and we feel sure that without a roentgenological examination it would have been impossible to make a diagnosis in this case.[1]

[1] In this connection, I would recommend for further and more detailed discussion of the abnormalities of the diaphragm, E. G. Stoloff's "The Chest in Children", *Annals of Roentgenology*, XII, Paul B. Hoeber, New York City.

VARIATIONS OF THE BONES OF THE WRIST

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VARIATIONS of the bones of the wrist were studied by anatomists before the discovery of the roentgen ray and their interest was directed largely to the relation of these variations to embryology and comparative anatomy. When roentgen examinations of injuries of the wrist came to be used, the surgeon and the roentgenologist became interested in the relation of these variations to surgical conditions and they were commented on in the literature. Comparatively little has been written on the subject in American roentgen literature, particularly in recent years.

A brief review of the literature will be given with a more detailed discussion of some of the variations that are of greatest interest to the roentgenologist. The variations that have occurred in the roentgenograms of the wrists of 1,452 individuals who were examined in a hospital practice during the past eight years will be reported. The actual number of wrists examined during this eight-year period was 1,841 but 389 cases were excluded from the series because of crushing injuries or because the films did not visualize all the bones of the wrist sufficiently well to permit of a complete study

A knowledge of the fundamental work of Pfitzner[11,12] is necessary for a correct understanding of the variations which occur in the bones of the wrist. Dwight[4] in his monograph gives a complete summary of Pfitzner's plan of the hand, and for detailed information the reader is referred to this monograph. The following is a brief résumé of Pfitzner's plan of the bones of the wrist.

I. An antibrachial row
   1. Triangulare.
   2. Secondary pisiform.
II. A proximal row.
   1. Radial navicular.
   2. Ulnar navicular.
   3. Lunate.
   4. Radial triangular.
   5. Ulnar triangular.
   6. Pisiform.
III. Central row, none of which normally persist as a separate bone.
   1. Radiale externum.
   2. Epitrapezium.
   3. Centrale.
      (a) dorsal element.
      (b) palmar element (of minor importance).
   4. Epilunatum.
   5. Hypolunatum.
   6. Epipyramis.
   7. Ulnare externum.
IV. Distal row.
   1. Trapezium.
   2. Trapezoid (palmar half).
   3. Metastyloid.
   4. Hamate.
V. Carpal-metacarpal row, none of which are normally seen as a separate bone
   1. Paratrapezium.
   2. Praetrapezium.
   3. Secondary trapezium.
   4. Secondary trapezoid.
   5. Epitrapezoid—essentially the greater part of the dorsum of the trapezoid.
   6. Parastyloid.
   7. Styloid.
   8. Subcapitatum.
   9. Secondary capitate.
   10. Bone of Gruber.
   11. Hamular bone.
   12. Bone of Vesalius.

Pfitzner also published in Grashey's Atlas schematic charts of the dorsal and palmar aspect of the wrist in which the approximate location of the numerous accessory bones is indicated; these have been reproduced by Köhler.[8] These charts and that of Thilenius[16] have been used in reproducing the illustrations given here (Figs. 1 and 2). Such charts are of value to the roentgenologist in identifying anomalies, but it should be remembered that most of these bones are rare, many of them have never been seen on a roentgenogram and it would be difficult or impossible to

demonstrate some of them if they did occur. Some anatomists have disputed the existence of certain of these elements, but Pfitzner's classification remains the best working basis for an understanding of these variations.

Each of the bones of the wrist will be discussed and the embryological elements forming it mentioned, together with the accessory bones that may be the result of a departure from the usual developmental course.

The *centrale* is listed by Pirie[13] as a moderately rare bone. It was observed by Pfitzner[12] 7 times and by Grumbach[6] 3 times. It has a separate center of ossification[7] and usually forms a part of the navicular. It more rarely unites with the capitate or, still more rarely, with the trapezoid. When it disappears completely and its place is taken by fibrous tissue there is a striking open space between the capitate and the navicular. While no separate centrale was demonstrated in my series there were 9 instances of this striking space where the centrale should have been located (Fig. 3). Most of these roentgenograms showed a marked indentation of the capitate and this was located farther away from the navicular than the majority of authors describe the location of the centrale.

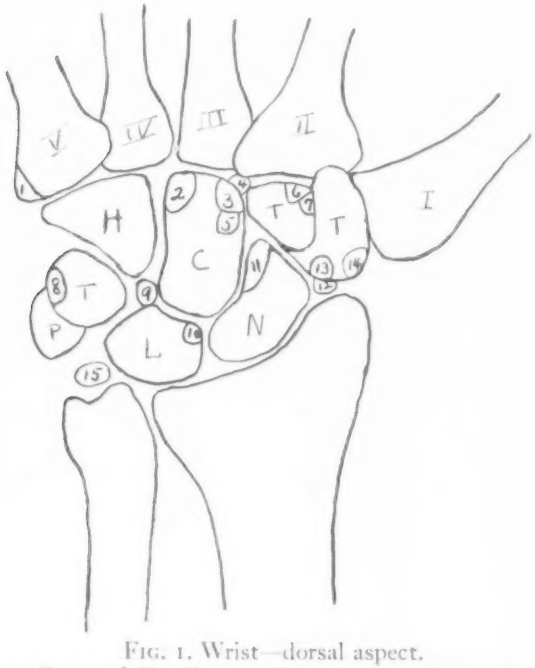

Fig. 1. Wrist—dorsal aspect.

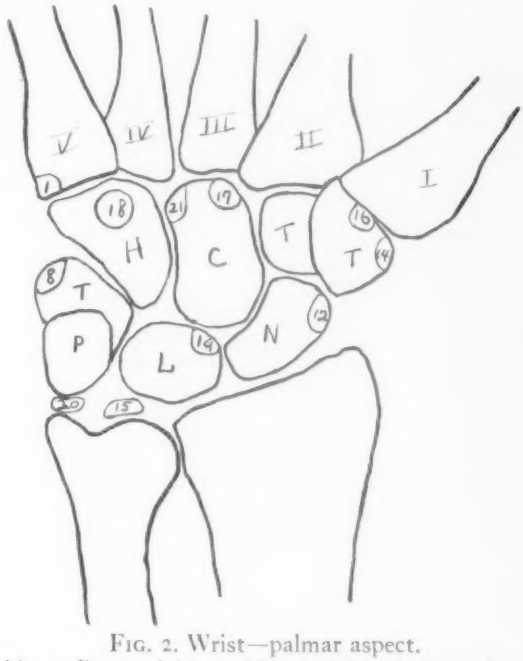

Fig. 2. Wrist—palmar aspect.

1. Bone of Vesalius. 2. Secondary capitate. 3. Styloid. 4. Parastyloid. 5. Metastyloid. 6. Secondary trapezoid. 7. Secondary trapezium. 8. Ulnare externum. 9. Epipyramis. 10. Epilunatum. 11. Centrale. 12. Radiale externum. 13. Epitrapezium. 14. Paratrapezium. 15. Triangulare. 16. Praetrapezium. 17. Subcapitatum. 18. Hypolunatum. 19. Hamular bone. 20. Secondary pisiform. 21. Bone of Gruber.

NAVICULAR

The navicular bone is formed of a radial and an ulnar element, of the radiale externum, the centrale, and occasionally of the epilunatum.

The *radiale externum* rarely occurs as a separate bone. In my series one film showed a projection on the outer side of the tuberosity of the navicular which undoubtedly represented a fused radiale externum which had not been as completely incorporated in the tubercle as usual, but no instance of a separate bone was found.

Various authors differ in their interpretation of the *divided navicular*. Pfitzner[12] described the divided navicular and believed that a true fracture of the navicular never occurred. Dwight states that undoubtedly the divided bone can result from failure of

Fig. 3. Space for fibrous centrale.

the two elements to unite, while Köhler says that Pfitzner's divided bone has never been proved embryologically and that the mere presence of two pieces of bone does not prove that they were not traumatic in origin and that these findings are always the result of trauma. Grumbach also thinks that the divided navicular is always traumatic in origin. Dwight, while admitting that most of the specimens of divided navicular have a pathological appearance and that examples of this variation are often traumatic in origin, believes that many of these fractures are found in cases where there was a pre-existing divided navicular, or at least a bone with an incomplete fusion of the two elements. Gruber[5] found a divided navicular once and a triple navicular twice in 400 navicular bones. Pfitzner[12] found a complete separation of the navicular 9 times and an incomplete separation 13 times in 1,493 cases. In the 1,452 films examined by me 4 instances of a divided navicular were encountered (Figs. 4 and 5). In all of these the elements were clearly separated and there was no displacement between them. In 2 instances there was a definite negative history concerning trauma over the wrist. In the other 2 cases this point was not mentioned in the history and the patients were not available for questioning at the time the survey was made. In the same series 3 fractures of the navicular were noted in which there was displacement between the fragments.

LUNATE

The lunate bone is made up of a chief center, of the epilunatum, and the hypolunatum. The *epilunatum* may rarely be found as a separate bone on the dorsum of the hand in the angle between the navicular, lunate and capitate bones. This bone might easily be missed in a film of the wrist made in the usual position with the palmar surface down. Dwight gives an illustration of a separate epilunatum found in an anatomical specimen. He states that very rarely the separate epilunatum may undergo abnormal development with a corresponding decrease in the size of the lunate. This fact offers an explanation of the apparent division of the lunate into a dorsal and palmar element which has been described. The *hypolunatum*, which is on the

Fig. 4. Divided navicular.

palmar surface of the hand, is of rare occurrence and has no practical importance. No example of an epilunatum or a hypolunatum was found in this series.

TRIANGULAR

The triangular bone is composed of a principal center, of the epipyramis, and the ulnare externum. Pfitzner[11] says that the main part of the bone is composed of a radial and an ulnar element. Separate centers of ossification for the two centers do not exist and Dwight does not recognize them. The *epipyramis* rarely occurs as a separate bone and when it does is found on the dorsum of the hand between the lunate, triangular and hamate. Grumbach observed this bone 3 times and Heimerzheim[7] once. No example was found in this series. The *ulnare externum* is also occasionally seen as a separate bone and is located on the dorsum of the hand on the ulnar side between the tuberosity of the fifth metacarpal and the triangular and lunate; Pfitzner[12] found it once and Grumbach twice. None was seen in this series.

Fig. 5. Divided navicular.

Fig. 6. Fused secondary pisiform.

PISIFORM

The pisiform bone varies considerably in size, shape and position but there are no variations that are of particular interest to the roentgenologist. The secondary pisiform, the triangulare, and the separate styloid process of the ulna will be discussed.

The secondary pisiform is very rarely found as a separate bone. It is located close to the pisiform between the pisiform and the tip of the styloid process of the ulna. Dwight stated that no separate bone had been demonstrated at that time but that he had an anatomical specimen showing a distinct articulating facet on the pisiform and he felt reasonably sure that a separate secondary pisiform had been present in

Fig. 7. Triangulare.

this case. One example of a secondary pisiform was found in my series and one other plate showed a distinct projection from the pisiform which probably represented a secondary pisiform that had become fused with the pisiform (Fig. 6).

The *triangulare bone* was found by Thilenius[15] in 65 per cent of embryos at the second month but it occurs very rarely in adults as a separate bone. It is located between the radius and ulna on one side and the lunate and triangular on the other side. Pfitzner[12] found bilateral bones in 2 instances. Lilienfeld[9] found it as an accessory bone 3 times in 400 roentgenograms. Grumbach doubted the existence of such a bone and in 800 roentgenograms saw no evidence of it. Schinz[14] expresses the opinion that most, if not all, of the so-called examples of the triangulare bone are old fractures of the styloid process of the ulna with formation of a pseudo-joint. Heimerzheim, while admitting that many fractured styloid processes are mistaken for triangulare bones, does not deny the existence of the bone. Köhler, although believing that trauma plays an important part in the production of the condition commonly reported as a triangulare bone and that embryological data are inconclusive, does not deny that Pfitzner's 2 cases were true triangulare bones. Two films were found in my series that appeared to be examples of the triangulare bone (Fig. 7). These accessory bones were placed between the tip of the styloid process and the pisiform bone well away from the styloid process and both cases showed normally shaped and well-developed styloid processes. This location is not exactly as described by Pfitzner and these bones did not possess the flattened shape described by him. There was no history of trauma to the wrist although it must be remembered, as Köhler has pointed out that such a slight injury as a twist of the wrist may result in a fractured styloid process and that such slight trauma may not be remembered by the patient at a later date.

Most standard books on anatomy do not

Fig. 8. Separate styloid process of ulna.

Fig. 9. Separate styloid process of ulna.

describe a separate center of ossification for the styloid process of the ulna. Schwegel in 1858 (quoted by Köhler) described a separate ossification center which occasionally occurred in the styloid process, and Merkel[10] also described a separate center and stated that very rarely it fails to unite, thus forming a separated styloid process. Two very definite examples of this variation were found in this series and the films were so characteristic that there can be no doubt in regard to the interpretation of the findings (Figs. 8 and 9).

TRAPEZIUM

The trapezium is composed of a chief center, of the praetrapezium, the secondary trapezium, the epitrapezium, and the paratrapezium. All of these accessory centers of ossification may form separate centers but all are of rare occurrence.[4] When they do occur the *praetrapezium* is located on the distal end of the tuberosity on the palmar surface, the *secondary trapezium* at the ulnar distal angle of the trapezium, the *epitrapezium* on the dorsal side next to the navicular and the *paratrapezium* at the outer distal angle of the trapezium. None of these bones were found in this series.

TRAPEZOID

The trapezoid presents very little of interest to the roentgenologist. It may rarely be found divided into a dorsal and a palmar half with the palmar half reaching the dorsum at the radial side. Occasionally the styloid becomes fused with it. Pfitzner[12] in his series of 1,493 cases found it so fused 16 times. I found only 2 unmistakable examples in 1,452 roentgenograms.

CAPITATE

The capitate is composed of a main center of ossification of the secondary capitate, and the subcapitatum. The styloid is sometimes fused with this bone. The *secondary capitate* is located at the distal ulnar dorsal angle of the capitate. Dwight reports it as having been seen separate twice. The *subcapitatum* has been seen separate once.[4] It is located on the distal end of the palmar surface of the capitate. Pfitzner[12] found the styloid incorporated in the capitate 54 times but I found only 7 instances in which it was definitely demonstrated on the films.

Gruber's bone is very rarely found and is a small pyramidal-shaped mass lying between the base of the third and fourth metacarpals and the capitate and lunate.

HAMATE

The hamate bone is made up of the bone proper and the hamular bone. There is considerable variation in the size of the hamular process which is formed by the *hamular bone* and it may occur as a separate bone on the palmar surface. It is not easily demonstrated on the roentgenograms and in the lateral position may suggest a fracture. Dwight had never seen an example of this bone. One film was found in my series that did show a separate hamular bone.

The remaining accessory carpal bones are more intimately associated with the

metacarpals than the carpal bones and will be discussed with them.

METACARPALS

The metacarpals are formed from one chief center of ossification and one epiphysis which is located at the proximal end of the first and the distal end of the other four. There may occasionally be an additional epiphysis at the proximal end of the other metacarpals. This occurs most frequently in the second and next most frequently in the fifth metacarpal. In my series of 1,452 wrists only 448 were in persons young enough to show the ununited epiphysis on the roentgenogram, yet 8 examples of an epiphysis at the proximal end of the second metacarpal were found. This is a greater incidence than has usually been recorded. Dwight reports only one instance and while most writers do not state the frequency of occurrence they leave the impression that it is very rare. No examples of an epiphysis were found at the proximal ends of the other metacarpals.

Fig. 10. Fusion of lunate and triangular.

The *secondary trapezoid* was reported by Dwight to have been seen separate 5 times. It is located on the dorsum and represents the tip of the radial side of the base of the second metacarpal. The *parastyloid* was seen separate once by Dwight and is usually represented by an ulnar projection on the dorsum of the base of the second metacarpal. The *styloid* is difficult to demonstrate on the roentgenogram when it occurs separately and Dwight saw only 2 instances that were definite. It forms normally the styloid process of the third metacarpal. The *metastyloid*, which is also very uncommon, occurs on the dorsum between the point of the styloid process of the third metacarpal and the capitate and trapezoid. The *bone of Vesalius* forms the tip of the ulnar side of the base of the fifth metacarpal. Its separate occurrence is rare. None of this group of accessory bones were seen in my series.

FUSION OF CARPAL BONES

Dwight gives a very good summary of this subject, and Cave,[1] in 1920, reviewed the literature and reported a case of bilateral fusion of the capitate and trapezoid together with the styloid element of the third metacarpal. Non-pathological fusions are relatively rare.

Fusion of the *navicular* and *lunate* was never observed alone by Dwight. One example was found in this series.

Fusion of the *lunate* and *triangular* is relatively rare but 2 examples of this variation were found (Fig. 10).

Fusion of the *triangular* and *pisiform* rarely occurs alone and when general pathological fusion occurs it is the last to take place. One example was found in this series.

The *trapezoid* and *navicular* have been found fused once but no example of this anomaly was found.

The *trapezoid* and *capitate* were reported fused twice by Dwight and 2 examples of this fusion were found in this series (Fig. 11).

The *capitate* and *hamate* were seen fused in 2 cases by Dwight and 3 instances of

complete fusion and 3 of incomplete fusion were found in this series. One of the cases showing complete fusion was associated with fusion of the trapezium and trapezoid.

It is difficult to demonstrate fusion of the *trapezium* and *trapezoid* on a roentgenogram but two films were found where the findings so definitely indicated this fusion that they were classified as such.

Dwight reported the fusion of the *second metacarpal* and *trapezoid* in 3 instances but none were found in this series. He also reported the fusion of the *third metacarpal*, *capitate*, and *trapezoid*.

A study of the sesamoid bones was not made. The reader is referred to Dwight who gives a very good summary of their occurrence.

Many of the variations which have been discussed are so rare that they are mere curiosities. Some are situated so that they would not be mistaken for fractures but others are of definite medicolegal importance.

Pfitzner's plan of the hand has been followed but it should be remembered that many anatomists do not recognize all of these elements. Roentgenologists will do well to remember the admonition of Köhler, based on the work of Grumbach, that the *centrale*, *secondary pisiform*, *secondary trapezoid*, *styloid* and possibly the *ulnare externum* are universally accepted as accessory elements embryologically while the others are not so recognized. Grumbach was undecided whether or not to include the *epitrapezium* and *epipyramis* in this group. He believed that he had definitely shown that the *divided navicular* and the *triangulare* were traumatic in origin but other workers have failed to support his contention, and my personal belief is that the position of Dwight is more nearly accurate: that these variations may occur but that traumatic lesions are often mistaken for them by the novice. Grumbach grouped elements together about which he could obtain little information regarding their possible traumatic or inflammatory origin; they were the *radiale externum*, *epilunatum*, *hypolunatum*, *triangular bipartium*, *secondary trapezium*, *divided trapezoid*, *metastyloid*, *parastyloid*, *subcapitatum*, *secondary capitate* and *Gruber's bone*. He made a further group of the *styloid*, *hamular bone* and the *bone of Vesalius* which might be expected to exist from studies in comparative anatomy and embryology but which have never been definitely demonstrated to his satisfaction. What appears to be a separate hamular bone was shown on a film in this series.

Fig. 11. Fusion of trapezoid and capitate.

SUMMARY

A brief summary of Pfitzner's plan is given together with a review of the literature dealing with the occurrence of variations of the bones of the wrist.

The variations found in a review of the roentgenograms of the wrists of 1,452 individuals is given. These variations are as follows:

Divided naviculars—4
Spaces for fibrous remains of the centrale—9
Secondary pisiform—1
Triangular bones—2
Ununited styloid process of ulna—2
Hamular bone—1
Epiphysis at proximal end of second metacarpal bone—8

Fusions:
Navicular and lunate—1

Lunate and triangular—2
Triangular and pisiform—1
Trapezoid and capitate—2
Capitate and hamate—3 (one associated with fusion of trapzeium and trapezoid.)
Apparent trapezium and trapezoid—2

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DECALCIFICATION OF SELLA TURCICA DUE TO MALIGNANCY AND RECALCIFICATION OF SELLA AFTER ROENTGEN THERAPY*

CASE REPORT

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IN GOING through the literature, I could find no instance of a recalcification of the sella turcica by roentgen therapy once it had been rendered invisible by decalcification due to malignancy. At a recent neurological meeting in Philadelphia, Dr. Kornblum made the statement that the sella, once decalcified, does not recalcify. I am giving here the report of a case that shows that the sella may recalcify following roentgen therapy.

Miss H., aged forty, a teacher of the deaf and dumb, was referred to me by Dr. Phillip J. Lewert, laryngologist, for roentgen treatment. The patient had enlarged lymph nodes and swelling of the right side of the neck, starting behind the right lobe of the ear and extending low down to the clavicle. The left side was also involved in a similar manner but not so marked. The patient complained of occipital pain, disturbances of vision (double at times). Hearing was impaired and dizziness encountered when sitting up or reclining.

History of Illness. November 15, 1924, the patient called at her family physician's office with a cold in its first stage, malaise and muscle pains. Diagnosed grippe. On November 17 she went to bed with aggravation of symptoms. Within a few days a sore throat and cervical adenitis developed. She was in bed for about four weeks, running a little fever at times. Toward the end of this illness she developed a hoarseness which did not seem to yield to local treatment, but which passed away in about ten days. After getting out of bed she still complained of sore throat, and an examination revealed a punched out ulcer on the right anterior pillar. In January, 1925, the patient began to notice a gradually increasing diplopia. Within a short time there was a noticeable internal strabismus. In early December while still in bed with grippe the patient began to complain of occipital headaches. These have gradually increased in severity to date. About a week ago she began to complain of nausea and has vomited several times. This vomiting has not been of the cerebral type.

Family History. Negative.

Past History. Rheumatism (rheumatic fever) three years ago. Was in bed six weeks. Tonsillectomy two and a half years ago. Otitis media, right, October, 1923, and December, 1923. Ear drums opened on both occasions. No mastoid trouble.

On January 10, 1925, the patient received roentgen exposures through three ports of entry, on each side of neck, starting behind the lobe of the ear, working down to the clavicular region. These treatments were given in one sitting, making a total of six exposures. On January 31, 1925, the patient returned. She was able to walk and travel around with a companion. Her throat condition described above and the swelling of the neck had improved. The ulcers were partially healed but the diplopia, headache and nausea were aggravated. The patient still vomited at times, but not projectile. Because these symptoms were so alarming, I took a roentgenogram of the head and chest, which revealed the chest negative for metastasis. The head showed the sella turcica partially visible. The floor was irregularly outlined and the posterior clinoid processes were hardly visible. With this report, I urged the laryngologist to have the patient referred to Dr. William Spiller, who admitted the patient on March 4, 1925, to his service in the Hospital of the University of Pennsylvania.

Dr. Lewert's report, February 26, 1925. "Miss H. was referred to me by her family physician, the early part of January, 1925, for a throat examination, he having noticed a lesion in the pharynx. Examination revealed a punched out area at the posterior edge of the soft palate between the base of the uvula and upper part of the right tonsillar fossa (tonsils are absent). The base of this lesion presents a

* Read before the Third International Congress of Radiology, Paris, France, July 25–29, 1931.

nodular, scarred appearance, and seems to extend somewhat into the upper part of the right tonsillar fossa. There has evidently been some scar contraction, as the uvula is drawn to the right, and the right lateral region of the pharynx

FIG. 1. Partial destruction of the sella turcica due to malignancy. February 25, 1925.

is diminished in size. The lesion is not granulated and does not bleed readily on manipulation. There is a large swelling easily palpable on the right side of the neck, apparently adherent to underlying structures, this mass being just below the angle of the mandible and extending forward, backward and downward from that location. A similar mass occupies the left side of the neck in about the same location but is very much smaller, being possibly half the size of a walnut. These enlargements are not particularly sensitive to the touch. The patient says that she had an attack of grippe about a month previous to this visit, during which time the swelling in the neck was so great as to resemble parotitis, but had subsided somewhat. A tentative diagnosis was made of malignancy with secondary involvement of the cervical lymphatic glands."

Dr. Spiller's report, March 20, 1925. "Two weeks ago the patient had a spinal puncture. This aggravated the headache and she has been in bed ever since. Has retained little food in past four days. Now has vertigo on attempting to stand. No flashes of light or hallucinations of smell. No paresthesias, paralyses (except of ocular muscle), no convulsions. There is ringing in the ears, gradual failure of vision and increasing deafness." Dr. Spiller agreed that the patient was suffering from a malignant growth, affecting each side of her neck and causing intracranial involvement.

While at the University Hospital, Dr. Pancoast also roentgenographed the region of the sella turcica and he reports: "There is still some dorsum sellae left, the pituitary fossa is about top normal size. AP–12 mm. There is a suggestion of rarefaction throughout the pituitary region." (See Fig. 1.)

Dr. George Fetterolf, laryngologist of the University Hospital, reports: "March 10, 1925. Nose, slight irregularity of septum; turbinates negative. Sinuses, frontal clear, maxillary clear. Nasopharynx, landmarks much distorted but this much can be seen: Considerable edema of ostia of both eustachian tubes, expecially of the right. Much swelling around the right half of the nasopharynx with protrusion of the anterior wall of the sphenoid and the mesial wall of the posterior ethmoid group. Soft palate: Marked restriction of muscular action of the left side, almost complete immobility of the right side. Ulcerating lesion involving right half from margin up to attachment of soft to hard palate. Believe there is present a malignant growth which began probably in the right spheno-ethmoid and has extended to the soft palate to the opposite sphenoid and endocranially."

Report of Dr. Alexander G. Fewell, March 18, 1925. "Ocular movements are normal, pupils equal, regular and respond to usual reflexes. Rotary nystagmus in lateral rotations. Palpebral fissures apparently equal. Unable to map out diplopia fields carefully as patient became dizzy. There is no diplopia looking straight in primary position at two feet. Beyond this there is diplopia increasing in lateral rotation both to right and left. This would suggest a paralysis of divergence. O.D. Media clear. Overcapillarity of disc, with somewhat blurred margins, especially upper nasal border, which is hardly definable. The veins are over full, but not tortuous. There are no hemorrhages or exudates. O.S. Similar in all respects. Vessels are suspicious and should be watched for further signs of intercranial pressure. (See Fig. 2.)

On March 25 the blood count was as follows: red blood cells, 5,010,000; white blood cells, 10,200; hemoglobin, 105 per cent; neutrophiles, 70 per cent; lymphocytes, 23 per cent; large

mononuclears, 4 per cent; transitionals, 2 per cent; eosinophiles, 1 per cent. Wassermann reaction, negative.

After three weeks' study and observation, Dr. Spiller returned the patient to me for roentgen therapy.

April 11, 1925. Patient was not able to walk on account of weakness and dizziness. She was brought in an ambulance to my laboratory. While under treatment, the patient vomited and suffered from extreme headache. Eight exposures were given at one sitting. The small area covered the right and left temporal regions, back and sides of neck, centering the rays upward toward the sella. The patient was very much exhausted after the completion of these treatments. May 6, 1925, the patient walked into my office with some assistance, much stronger,

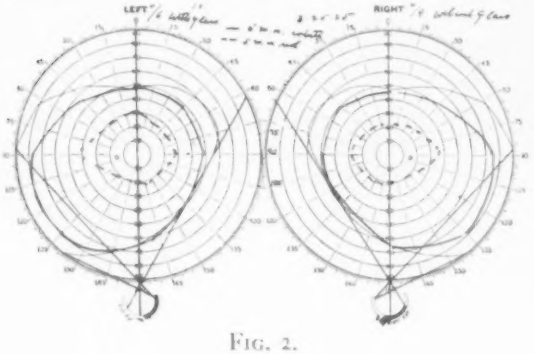

Fig. 2.

and less dizzy, but still complaining of headaches. This time she received twelve exposures, also at one sitting. June 10, 1925, there was a great improvement. She walked in without assistance, her hearing and sight had improved and the headaches had lessened. She could get on and off the table easily, without help and without distress. The treatment was spread over a period of three days. The patient stood the treatment much better than on previous occasions.

July 17, 1925. The patient had been to the sea shore and walked well, enjoying fairly good health. Another series of treatments was administered and check-up roentgenograms were made, which revealed that the sella turcica had recalcified. The bony density of the sella was much greater than in a normal skull, which showed that bone formation had taken place in the rarefied sella and the posterior clinoids were also well formed (Fig. 3).

The patient had roentgen alopecia over the area exposed, but the exposed skin was in a good condition. Greatly delighted with finding the calcified sella, I took the patient to Dr. Pancoast; he was greatly surprised at the remarkable results. He suggested that it would be safe to administer one more series. This the

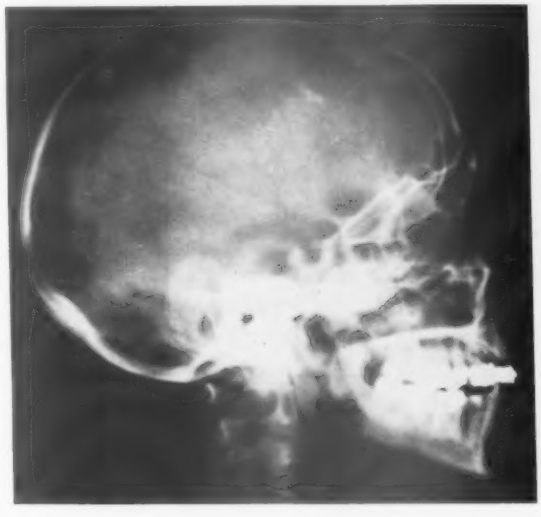

Fig. 3. Recalcification of the sella turcica after five months of roentgen therapy. July 17, 1925.

patient received on September 4, 1925. She returned every two weeks for observation. There was steady improvement for the next seven weeks. Then she began to fail, becoming rapidly worse, losing weight, with cachexia, enlargement of the cervical glands and symptoms of mediastinal involvement with marked emaciation. Death occurred on December 25, 1925. Unfortunately the family would not consent to a post mortem.

In the roentgen therapy of this case, the cross firing method was used. In all, the patient received 69 exposures, each field being 2×2 inches, 6 ma., 6 mm. Al and sole leather filter; distance, 8 inches; time, 6 minutes, spark gap, 8 inches.

CONCLUSIONS

This case shows that a decalcification of the sella turcica caused by malignancy can recalcify after roentgen therapy.

When operative measures are impossible, roentgen therapy should always be tried for palliative effect.

It is very important that roentgen therapy should always be followed and controlled by roentgenograms.

THE TIME-INTENSITY FACTOR IN IRRADIATION

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THE physical factors in radiation therapy have been subjected to searching investigation and refinement by physicists and radiologists. Filtration values and equivalents, the quality of the rays, their accurate measurement by instruments of precision have been studied assiduously. Teleroentgen therapy and teleradium therapy, or the application of radiation at relatively great distances, are in use, as are therapeutic roentgen-ray units of 900,000 volts. In another field, pathologists have acquainted us with detailed knowledge of the different radiosensitivities of tumors and of radiation effects on normal tissues. Intermediate between these physical and pathological studies are many unsolved biophysical problems, not the least important of which is the significance of the duration of irradiation—the so-called "time factor."

Some radiotherapists do not attribute much importance to the factor of time. As an example of this opinion we quote from a recent book on "Practical X-Ray Treatment" by A. W. Erskine: "It seems to be fairly well established that the rate at which x-rays are administered does not matter. The biological effect is a function of the energy expended and if, for instance x-rays are produced for one minute by 100 ma., the result will be the same as when they are produced for 100 minutes by one ma., all other factors being the same in both cases." In agreement with this opinion, we recall that the Committee appointed by the League of Nations to investigate various aspects of radiotherapy have not obtained sufficient clinical data to settle the question whether in the radium treatment of malignant tumors the best results are obtained with protracted radiation of small intensity or with brief radiation of great intensity.

As an example of the way the time factor is ignored, we may consider the computation of dosage as generally employed. From the point of view of quantity of radiation, the dose is determined by the product of time and the intensity of radiation, regardless of the range in these factors. In other words, without modifying the product one may vary either the intensity or the time, on the condition that a compensation of the variation of the one by an inverse variation of the other be made. It is possible (and even probable) that the ensuing biological reaction is dependent not only on the total energy delivered but also on the rate at which it is incident upon the tissue. The notation of dosage makes no allowance for this fact, unless the duration of the treatment is also stated.

It seems logical to assume that a cancer cell or a tissue cell would not be indifferent to variations in the intensity of radiation. Such a cell, continuously engaged in self-repair, the ingestion, consumption and storage of food, the excretion of waste products, the pursuit of its specific function, and possible preparation for cell division, and in delicate ionic balance with the tissue juices which bathe it, is a living unit and must be capable of making certain adjustments to the influences of noxious agents to which it is exposed, whether they be chemical or physical. All physiological processes require time for their completion. If the doses were equal, the cell—either normal tissue cell or cancer cell—should be more tolerant of prolonged irradiation of low intensity than of short irradiation of high intensity. This theory

* Read in a Symposium on the Biological Effects of Radium Radiation at the Sixteenth Annual Meeting, American Radium Society, Philadelphia, June 8–9, 1931.

is substantiated by abundant experimental proof.

The following two statements are generally accepted as biological truths: (*a*) the susceptibility of any cell to irradiation varies considerably during the lifetime of the cell and (*b*) different cells (e.g., cancer cells and normal tissue cells) vary greatly in radiosensitivity. When these cells are irradiated, the radiosensitive and radioresistant cells alike respond with greater effects to higher intensity and shorter duration of irradiation, but it is conceivable that while the response is comparable in kind it is not necessarily so in degree. The end-result of successful external irradiation is the destruction of the cancer cell and the preservation of normal tissue cells; there is experimental and clinical evidence to indicate that long duration and low intensity of irradiation (within limits) has greater differential effects on tumor cells than on normal tissue cells.

In the succeeding pages, we shall review the experimental data of other investigators on the time factor in irradiation and present additional evidence of our own. A majority of these investigators cited conducted their researches on the simpler forms of animal and vegetable life, following closely the lead of Lopriore, the first student in radiophysiology, who in 1897 demonstrated for the first time the influence of roentgen rays on tissue growth. He observed inhibition or arrest of growth after irradiating two plants—*Genista* and *Darlingtonia coronillaefolia*. Among the different test media which have been employed in the study of the time factor are: (*a*) chicken, frog, *Ascaris* and *Drosophila* eggs, (*b*) germinating beans, lentils and peas, (*c*) paramecia, (*d*) bacteria, (*e*) tissue cultures, (*f*) tumor implants, (*g*) human and pig skin, (*h*) corneas of urodele and rabbit, (*i*) anus of rat and (*j*) testicle of rabbit.

In Table 1, is given a summary of the experimental data found in the literature, grouped according to the findings. The range of values of the time-intensity factors is listed whenever it has been stated. The more significant papers will be discussed individually.

TABLE I

SUMMARY OF EXPERIMENTAL DATA ON THE TIME FACTOR IN IRRADIATION

A. Alterations in the factors of time and intensity (in the limits of these experiments) have no significance in the application of a given dose.
1. Ancel and Vintemberger. Fertilized chicken eggs prior to incubation.
2. Dognon. *Ascaris*. Ratio 1:4.
3. Friedrich and Krönig. Human skin. Ratio 1:4. Human Ovary. Ratio 1:4.
4. Glocker, Rothacker and Schönleber. Bean (*Vicia faba*). Ratio 1:10.
5. Laser. Growth rate of tissue cultures.
6. Lazarus-Barlow and Beckton. *Ascaris* eggs.
7. Liechti. Anaerobic *Ascaris* eggs.
8. Packard. *Drosophila melanogaster* eggs. Ratio 1:4.
9. Sievert and Forssberg. *Drosophila* eggs. Ratio 2.1:1800.

B. Greater effects with less intensity and longer duration of irradiation.
1. Nather and Schinz. Tumor implants.
2. Politzer and Alberti. Urodele cornea.
3. Rados and Schinz. Rabbit cornea.
4. Zuppinger. *Ascaris* eggs.
5. Wood and Prime. Grafts of Ehrlich mouse sarcoma. Flexner-Jobling rat carcinoma and Crocker mouse carcinoma (*in vitro*).

C. Greater effects with higher intensity and shorter duration of irradiation.
1. Ancel. Germinating lentil seeds.
2. Ancel and Vintemberger. Fertilized chicken eggs after incubation. 2 to 9 hours.
3. Arntzen and Krebs. Sproutings of common pea.
4. Canti. Numbers of mitoses in tissue culture.
5. Cox. Mitotic activity and length of survival of tissue cultures from choroid and sclera of chick embryo.
6. Crowther. *Colpidium colpoda*.
7. Friedrich and Krönig. Frog eggs. Ratio 1:50. Human skin. Ratio 1:8.
8. Holthusen. *Ascaris* eggs. Ratio 1:8:64.
9. Jüngling. Bean sprouts (*Vicia faba*). Ratio 1:6.
10. Lazarus-Barlow. Rectum of rat.
11. Liechti. Aerobic *Ascaris* eggs. Human skin. Pig skin. *B. pyocyaneus* and *B. prodigiosum*.
12. Markovits. Paramecia. Ratio 10:336.
13. Martius. Bean sprouts (*Vicia faba*). Ratio 1:4.
14. Matoni. Bean sprouts (*Vicia faba*). Ratio 1:4.

15. Mottram, Scott and Russ. Mitotic changes in transplanted Jensen's rat sarcoma.
16. Packard. *Drosophila melanogaster* eggs. Ratio 1:10.
17. Roesler and Henshaw. *Drosophila* eggs. Ratio 1:18.
18. Schwarz. Human skin.
19. Seitz and Wintz. Human skin.
20. Spear. Mitotic activity and length of survival of tissue cultures from embryonic choroid of chick.

D. Greater differential effects on tumor than on normal tissues with longer duration and less intensity of irradiation.
1. Juul. Transplanted Krebs' adenocarcinoma of mouse.
2. Regaud. Testicle of rabbit.
3. Samssonow. Transplanted sarcoma of rat.
4. Schinz and Slotopolsky. Testicle of rabbit.

I. REVIEW OF LITERATURE WITH COMMENTS

A. *Alterations in the Factors of Time and Intensity (in the limits of these experiments) Have no Significance in the Application of a Given Dose*

The Bunsen-Roscoe law of the photochemical action of radiation postulates that the product of time and intensity produces a constant effect. This law, also called "the reciprocity law," was stated by Bunsen and Roscoe in 1862, viz.,—"Equal products of intensity and time of exposure produce equal blackenings of photographic silver chloride papers of equal sensitivity." The symbolic representation ordinarily given is that in producing a constant effect $IT=K$, in which I is the intensity, T the time and K the constant effect. Bunsen and Roscoe found their law to hold over a range of intensities from 1 to 45. *A priori* one would not expect the law to obtain for extreme values of either I or T. This law is not universally applicable to biological material used as indicators of these effects. The validity of the Bunsen-Roscoe law for the phenomenon of phototropism was proved by Loeb.

Glocker, Rothacker and Schönleber exposed bean sprouts (*Vicia faba*) to roentgen rays and demonstrated the applicability of the law of Bunsen for intensities in the ratio of 1 to 10. Their experiments were performed with very small numbers of beans and cannot be considered accurate. Packard also found this law tenable within the limits of his investigations, involving the use of 50,000 eggs of *Drosophila* (fruit fly).

Laser studied the effect of beta and gamma rays from mesothorium on the growth rate of tissue cultures and concluded that the inhibition of growth caused by irradiation is independent of the factors of time and intensity involved.

Sievert and Forssberg have recently irradiated *Drosophila* eggs with 83 to 220 R and varying intensities of roentgen rays, the exposures varying from 3,600 to 2.1 seconds. They recognized as essential, in the investigation of the time factor, an appreciation of the variation of radiosensitivity in *Drosophila* eggs during the time of exposure to radiation. They found the death rate of the eggs of *Drosophila* to be affected equally if the dose of 165 R is given for any time whatsoever between 2.1 seconds and 1,800 seconds. The same result was also obtained when larger and smaller doses were used, at least within the dosage of 83 to 220 R in times exceeding five to ten seconds.

B. *Greater Effects with Less Intensity and Longer Duration of Irradiation*

Rados and Schinz produced ulceration of a rabbit's cornea by a dose of 10 skin erythema units given in seventeen to eighteen applications with intervals of two to four days. To cause the same effect by a single application, the dose had to be increased to sixteen skin erythema units; therefore they concluded that greater biological effects occurred with less intensity and longer duration of irradiation. Politzer and Alberti obtained similar results in their experiments on the cornea of the urodele.

In 1915, Wood and Prime studied the time factor in the irradiation of rat and mouse tumors, such as the Ehrlich mouse

sarcoma, the Flexner-Jobling rat carcinoma, and mouse carcinomas No. 11 and No. 180 of the Crocker Fund series. The tumor tissue was exposed *in vitro* to radium and then, with untreated fragments for controls, was inoculated into animals of the same strain. In one series of experiments a mixture of beta and gamma rays was used, with a time range of from one to five hours; in another, gamma radiation, with a time range from seven to thirty-six hours. In both cases they found a smaller amount of radiation necessary to kill the tumor cells when the lower intensities were used. The results, however, are not conclusive.

Contrary to the results obtained by Liechti and Holthusen (see below) Zuppinger irradiated *Ascaris* eggs and obtained a greater effect by irradiation of weak intensity over a long time. Zuppinger's error was probably due to his failure to consider the change in sensitivity of *Ascaris* eggs during the course of his experiments. *Ascaris* eggs divide very slowly and during cell division are much more susceptible to irradiation than in the resting stage. Holthusen showed with *Ascaris* eggs that definitely less damage was done by four intermittent doses distributed over ninety minutes and with equal intensity and equal duration of irradiation than when a single total dose was given.

The results of these researches by Rados, Schinz, Wood and Prime, Politzer, Alberti and Zuppinger are contrary to the great bulk of experimental evidence at hand.

C. *Greater Effects with Higher Intensity and Shorter Duration of Irradiation*

The first important studies on the time factor in irradiation were done by Krönig and Friedrich in 1918. With equal doses of gamma radiation and a difference of intensity from 1 to 4, they found no variation in the response of human skin. With equal doses of filtered roentgen radiation and a difference of intensity from 1 to 80 they found the higher intensity to produce a greater reaction in the human skin. The biological effect of irradiating frog eggs was more marked when the intensity was greater; in this experiment equal doses were used and the variation in intensity was 1 to 50. In the case of therapeutic irradiation of human ovaries for uterine fibromyomas and hemorrhagic metropathies, the clinical results were independent of the intensity of the roentgen rays within the limits of 1 to 4. From these data, they conclude that with differences of 1 to 8 in intensity, the biological effect is greater with the higher intensity.

In criticism of this research as well as many others in which similar conclusions have been drawn, we feel that the figures given for ratios indicating the variations in intensity are usually misleading. One investigator may show that a variation in the duration of irradiation from 1 to 10 will produce certain results, whereas another will show that the biological responses within the limits of this variation or ratio are the same in effect. These apparently contradictory results can be explained by the fact that the ratios of intensities employed are not significant unless the actual range of time used is stated. For example, in our own experiments (as we shall show later) if all the times used are short in comparison with the duration of the life cycle of the cell in question (i.e., a few seconds to a few minutes, or even several minutes to a few hours in certain cases), no difference will be observed with different intensities. If, on the other hand, the duration of exposure to the radiation of low intensity is comparable to the life time of the cell, a different result may be expected.

Canti, in his investigation of this problem, used the diminution of the number of cells in mitosis in tissue cultures as an indicator of biological effect. Sixteen batches of tissue cultures were divided into two lots of eight cultures each. One lot was kept as control and the other was irradiated with the planned dose, after which both lots were fixed and stained and the number of cells in mitosis in each culture was counted, those in the irradiated speci-

mens being expressed as a percentage of those in the control specimens. Various determinations were then made with different intensities of radiation for different times. From these results Canti concluded: (*a*) that there is a threshold of intensity below which no effect is obtained, however long the radium is left in place; (*b*) that there is a threshold of time for each intensity which must be passed before the effect is obtained. Canti interpreted his first finding as implying that under the conditions of his experiments, a larger amount of radiant energy is required if the exposure is long than if it is short.

Ancel and Vintemberger used chicken eggs as biological indices of the various factors in irradiation. Fertilized eggs not incubated were treated by single total doses and by broken doses distributed over eight hours time with no discernible difference in results. On the other hand, fertilized chicken eggs after incubating two to nine hours were more susceptible to the influence of a single intensive dose than to the same dose given in fractionated exposures. Several important deductions can be drawn from those experiments. Not only is the law of Bergonié and Tribondeau confirmed, but more important still, it suggests that variations in the factors of time and intensity can produce different results depending on the reproductive activity of the tissues irradiated. A similar experiment by Liechti on aerobic and anaerobic *Ascaris* eggs gave comparable results. Variations in the time and intensity of irradiation had little influence on the behavior of anaerobic eggs, which seemed to follow the Bunsen-Roscoe law, i.e., dependent on the product only of the time and intensity. *Ascaris* eggs in an aerobic medium, however, where their activity and preparation for reproduction were stimulated rather than inhibited, responded more readily to irradiation of greater intensity and less duration.

Cox employed tissue cultures as biological indicators to study the dosage factors of time and intensity. Tissue cultures from the choroid and sclera of chick embryos were grown in hanging drop slides and used for experimentation at the time of maximal mitotic activity. In *Part I* of this research, the effect of irradiation was measured by the variation in mitotic activity of the tissue within a short time after irradiation. The doses were such as would reduce mitosis to some fraction of the normal number without causing maximum inhibition. For small doses (25 R, 50 R, and 75 R), it was found that over the range of time and intensity employed, doses of long duration and small intensity were less effective in checking the mitoses than short doses of strong intensity. *Part II* of the investigation was concerned with the effect of irradiation as measured by the length of time the tissue survived after exposure to large doses of roentgen rays. For these large doses (3,000 R to 12,000 R) the survival of the tissue cultures subsequent to irradiation was used to determine the efficacy of the dose. A 2 to 1 variation of intensity had no appreciable effect on the changes induced by 3,000 R, while the same variation of intensity caused a dose of 12,000 R to be considerably more destructive at a larger intensity than at a smaller one.

Spear observed that the effect of gamma rays in reducing the number of cells in mitosis and on the survival period of tissue cultures (embryonic choroid of chick), after prolonged irradiation, was more marked with 300 mg. radium than with 100 mg., alteration in the duration of exposure being made so as to give a constant value to the product of time and intensity.

Mottram, Scott and Russ studied the changes produced in the mitoses of cells in Jensen's rat sarcoma, by radium radiation of various intensities. The augmentation of the time of irradiation with diminished intensity, the dose remaining constant, caused a very evident and constant diminution in the effect of the rays. Similar results with roentgen rays were obtained by Ancel with germinating lentil seeds and by Matoni with bean sprouts. Matoni's

experiments may be questioned because he employed as few as two seeds in some of his tests. The gauge of the effect of irradiation used by Matoni and Martius was the time of appearance of the secondary roots; this constituted a very accurate biologic test, because a difference of 5 per cent in the dose was said to register on this indicator. Arntzen and Krebs conducted similar experiments with common pea sprouts, giving the total dose at once and four fractionated doses of one-quarter skin unit each at intervals of four hours; the greatest damage to the pea sprouts was found to occur when the total dose was given at one exposure.

Roesler and Henshaw have conducted experiments which indicate that the time factor influences the killing of *Drosophila* eggs by irradiation, other conditions remaining the same. For equal doses, the higher intensities were found to be more effective. Essentially the same result was obtained with eggs one to one and a quarter hours old as with eggs four to five hours old.

Markovits exposed paramecia to mesothorium (equivalent in strength to 10 mg. of radium bromide). These protozoa were not killed by fourteen daily treatments of ninety minutes each. When he gave eight to ten hours of continuous irradiation at one exposure, the paramecia died, although the total dose administered was less than half the amount given by the fractionated irradiation.

The experiments of Schwarz have been confirmed in part by our own observations reported in the second part of this paper. Schwarz found in the roentgen reactions on the skin—the climax of which should be expected thirty-five days after irradiation—that the reaction to two partial doses separated by an interval of twenty-four or six hours or of *only two hours*, was far less than the reaction to total doses given in one session.

Holthusen has pointed out that two of the problems of practical dosimetry are concerned with (*a*) the length of time between treatments and (*b*) the actual duration of exposure to radiation. Holthusen's interrogations had best be quoted literally: "How do the same quantities of rays behave if administered with the same intensity but intermittently? What is the part played by the length of intervals between the individual partial doses and what is the part played by the size of the partial or fractionated doses themselves? Within what limits of time distribution are differences in effect still demonstrable? What

TABLE II

SUMMARY OF THE DIFFERENT EFFECTS OF FRACTIONATED DOSES OF IRRADIATION EQUAL TOTAL DOSES (HOLTHUSEN)

A. *Different Total Duration—Same Intensity*

Author	Object	Total Duration (Intervals)	Result
Wintz	Skin	Days	Large difference
G. Schwarz	Skin	Hours	Distinct difference
Jüngling	Beans	Hours	Distinct difference
Arntzen and Krebs	Peas	Hours	Distinct difference
Holthusen	*Ascaris* eggs	Minutes-Hours	Distinct difference
B. *Same Total Duration—Varying Intensity*			
Holthusen	*Ascaris* eggs	About 30 minutes	Difference just demonstrable
Friedrich	Frog larvae	Seconds	Distinct difference
Holthusen	*Ascaris* eggs	Fractions of seconds	No difference

happens when the total time of irradiation is the same but when in one case the partial dose is administered with great intensity and at long intervals and in the other case it is given with lower intensity and shorter intervals?"

Holthusen prepared a table to answer some of these questions. His data were obtained from his own experiments and those of Wintz, Schwarz, Jüngling, Arntzen and Krebs. This is reproduced as Table II.

Holthusen showed with his experiments on *Ascaris* eggs that definitely less damage was done by four intermittent doses distributed over ninety minutes with equal intensity and equal duration of irradiation than when a single dose was given. He also stated that a repetition of Bunsen and Roscoe's photographic experiments under these same conditions could give results similar to his own research with biological media: "The photographic effect of light of equal intensity depends also upon whether the light is sent out continuously or intermittently to the photographic emulsion. The weakening caused by intermittent irradiation is more marked when the ratio of the interval to the duration of the single irradiation is greater and when the quantity of light is less." (See Fig. 1.)

The principle of fractionated dosage has long been adopted in the treatment of many inoperable cancers, wherein the desired end-results are growth restraint of the cancer and preservation of the integument. The principle underlying the usage of fractionated dosage has been defined by Ewing as follows: "The cumulative effect of successive doses delivered upon cells rendered vulnerable by the hyperemia and degeneration excited by previous doses."

D. *Greater Differential Effects on Tumor Than on Normal Tissues with Longer Duration and Less Intensity of Irradiation*

Selective radiotherapy of cancer would take full advantage of the differential tolerance of cancer and normal tissues for roentgen rays and gamma rays. In other words, the radiotherapist must utilize every available means for profiting by the radiosen-

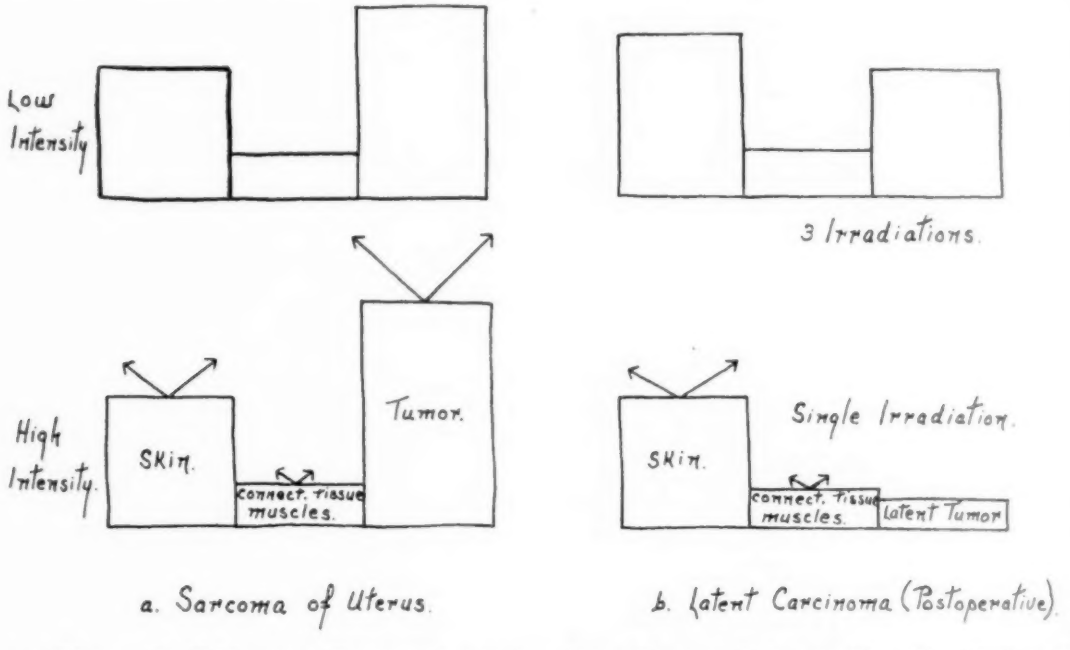

FIG. 1. Diagram by Holthusen to illustrate the relative effects of low and high intensities of irradiation with equal total dosage. Height of cube = tissue sensitivity to irradiation. Length of arrow = growth energy of tissues.

sitivity of the cancer being treated, and at the same time conserve the integrity of the more radioresistant normal tissues, particularly the skin, which may receive an equal or greater dose of radiation than the cancer itself. Therefore in submitting the biophysical factors in irradiation to experimental inquiry, we must consider, for practical purposes at least, not only the response of cancer to the different modifications of these factors but also the response of the normal tissues comprising the environment of the tumor. The tumor cannot be removed from the body for treatment by irradiation, therefore the maximum dose which can be delivered to it from external sources of radiation is limited entirely by the tolerance of the tissue which contains it. It is conceivable that the normal and cancerous tissues might vary considerably in their "differential" reactions to changes in the qualities of roentgen rays (e.g., wave lengths) or in the time of irradiation by roentgen rays or gamma rays. If such variabilities do exist, we should strive to ascertain what intensity or duration of irradiation would best afford a complete sterilization of the neoplasm with minimal injury to the adjacent normal tissues.

To the solution of this problem Regaud and his collaborators—Lacassagne, Coutard, Ferroux—have turned their ingenious talents, and compared the effects produced on the anorectal skin and mucosa and the testicular tissues of the rabbit, by selected doses of roentgen rays delivered in different times. The testicles of mammals were chosen for these experiments because their behavior and structure closely resemble that of malignant tumors, e.g., frequent cycles of cellular reproduction, active mitosis and radiosensitivity. This analogy between the mammalian testicles (in a state of active spermatogenesis) and malignant tumors is also apparent in their response to roentgen rays and gamma rays. In conducting these experiments they irradiated simultaneously (and under the same constant conditions) the two testicles of the rabbits; one testicle was removed in 260 days to eighteen months, the other was resected in four to five months; then they made a final comparison of the structure of the two organs, and so determined whether the cessation of spermatogenesis was temporary or permanent. In these experiments, Regaud employed a Coolidge tube of 180,000 maximum volts, filtration of 0, 3, 5 and 8 mm. of aluminum plus a plaque of wood 15 mm. thick, intensities of 2 to 8 milliamperes and target skin distance of 30 centimeters. The doses were measured in the R units of Solomon.

Nogier and Regaud, in 1911, were able to obtain complete sterilization of the testicles without skin lesions other than epilation, in the cat, dog and ram, by fractionated doses of roentgen rays. This result was obtained with lightly filtered roentgen rays of moderate penetrating power. Regaud also discovered in 1922 that a small dose of gamma rays administered continuously during a long time was more effective in inhibiting spermatogenesis in the ram than a dose of 5 times greater strength given in a very short time. There may be two sources of error in this experiment: the irradiation was given interstitially by radium puncture and therefore may have traumatized the testicle, and the testicles were not permitted to survive long enough to be certain of sterilization.

When Regaud applied a single small dose of roentgen rays (e.g., 2,000 Solomon R) to the rabbit testicles, he observed a pause in the reproduction of spermatogonia and a diminution in the number of cells comprising the seminal epithelium. This loss of cells was temporary; after several days or several weeks, depending on the dose, the spermatogonia regained their activity and insured the succession of generations. After a single dose of 3,500 to 4,000 R few spermatogonia survived. This dose caused only benign and transient lesions of the skin such as temporary alopecia and desquamation of epidermis. But if Regaud gave a greater dose (4,000 to 4,400 R) always by a *single* irradiation, severe radionecrosis of the integument in the anogenital region

of the rabbit followed, without complete sterilization of the testicle. He assumed therefore that *it was impossible to sterilize the testicles of the rabbit by the administration of a single massive dose of roentgen rays without causing serious lesions of the skin.* If this same dose (4,000–4,400 R) was properly fractionated, the skin changes were reduced to a temporary and partial epilation and moderate desquamation of the epidermis. Fractionation of a dose of 5,000 R, and augmentation of the total duration of treatment to four to sixteen days considerably diminished the effect of the roentgen rays on the anorectal skin but did not influence their effect on the seminal epithelium; hence it was possible by this means to administer to the rabbit testicle a dose sufficient to cause definite sterilization without injuring the anorectal integument. Regaud treated 6 rabbits with doses of 6,180 R; in 3 rabbits, wherein this dose had been fractionated in five, nine and thirteen days late radionecrosis ensued; in the 3 other rabbits, wherein this dose had been distributed in seventeen, twenty-five and thirty-three days, the cutaneous effects diminished in proportion to the prolongation of the time of exposure. Regaud has drawn the following conclusion from these experiments: "If, without altering any of the other experimental conditions, we modify the chronological distribution of the dose, dividing it and lengthening the time of its administration, we observe a remarkable difference between the effects produced on the integuments of the rectum and on those produced on the testicle. The effect on the integuments is attenuated and lessened while the effect on the testicle is increased."

These studies on spermatogenesis and similar clinical experiments on the roentgen and radium treatment of epidermoid carcinomas furnished Regaud with the data from which he formulated his theory of radiation therapy. His explanation of the superiority of continuous or fractionated irradiation over short intensive treatments is founded on the existence of alternating periods of radiosensitivity and of radioresistance in the life of the spermatogonia (in the experiments) and the cancer cell (in clinical practice). Spermatogenesis in a mammal such as the rabbit is a continuous phenomenon if the testicle is considered as a whole. But if one considers only a certain cell or line of cells on a seminiferous tubule, the function of reproduction by cell division is seen to be discontinuous and cyclic and the spermatogonia, like cancer cells, pass through alternating phases of multiplication (brief phases) and of rest (long phases). In one line of cells, therefore, either spermatogonia or cancer cells, the phase of multiplication corresponds to an accentuation of radiosensitivity (law of Bergonié and Tribondeau), whereas the phase of rest corresponds to a diminution in radiosensitivity. A short treatment therefore might destroy only those spermatogonia or cancer cells which are dividing at that time; it spares the others. It is only natural that prolonged and continuous irradiation (in the case of radium) or well-fractionated irradiation with proper spacing of the fractions into a fairly long time (in the case of roentgen rays) is more efficient than brief intensive irradiation, because in the first case the germinal or cancer cells are killed one after the other as the cycle progresses and these cells enter for the moment the phases of maximal radiosensitivity.

On account of this double alternating phenomenon of reproductive activity in the cell, a short irradiation will destroy only those cells which at the moment are in a state of maximal radiosensitivity. The ideal result is not only to cure cancer completely and definitely but to conserve the integrity of the less sensitive normal tissues. This effect can best be obtained, according to Regaud, by prolonging the time of treatment over five to twelve days. It is only in the stratified pavement epitheliomas of epidermoid origin, e.g., the skin and the orifices of the skin, mouth, larynx, vagina and cervix uteri, where prolongation of the time of treatment, according to

Regaud's plan, has proved efficacious. An apparent refutation of this principle might be found in the fact that epidermoid carcinomas of the skin and cervix are so amenable to radiation therapy that short intensive exposures to radium obtain a high percentage of cures. But if the radiologist compares the scarring of the skin and the stenosis and induration of the vagina, together with the occasional complications of late radionecrosis and rectal injury, with the flexibility of skin and vaginal vault which follows the less intensive irradiation, he will readily perceive the advantage of the latter method.

The clinical experiments of Jüngling, Béclère and Perthes in the postoperative irradiation of cancer of the breast indicate that recurrences are more frequent after intensive roentgen therapy than when smaller and more frequent doses are administered. In our experience it is only in the most radiosensitive tumors that a complete clinical disappearance follows a single exposure to a dose of radium or roentgen rays that does not destroy the normal tissues. These tumors, such as the lymphosarcomas, lymphoepitheliomas, thymomas, Wilm's tumors and transitional cell carcinomas of the oro- and nasopharynx, respond rapidly to almost any form of irradiation, but the most successful end-results have followed the prolonged irradiation of weak intensity.

Samssonow, working in Regaud's laboratory, studied the time factor in the irradiation of transplanted sarcomas in rats. A dose of 5,580 R given at one exposure was sufficient to sterilize the neoplasm but the animals died with radionecrotic ulceration of the skin. On the other hand, the tumor could be sterilized with survival of the animals and without serious skin lesions, providing the dose was of slightly less intensity, but fractionated in three parts administered on three consecutive days.

Schinz and Slotopolsky's experiments were similar to Regaud's, but their conclusions are somewhat fanciful. When the testicle of a sexually mature rabbit received 100 per cent of a skin unit dose by a single irradiation, the seminiferous tubules became denuded at first but recovered completely, then the complete degeneration ("emptiness") of the seminiferous tubules (except for the Sertoli cells) persisted for a very long time, recovered very slowly (incomplete thirteen weeks after irradiation) and in some parts of the organ spermatogenesis was never resumed. The fractionation of the dose considerably retarded the restitution of the atrophying testicle in contrast to the early recovery in the case of a single irradiation. The authors attribute this phenomenon to the development of allergy or anaphylaxis engendered by the necrotic spermatic cells against their own kind.

Juul studied the relation between the skin effect and the effect on transplanted tumors (Krebs' adenocarcinoma of mouse) from exposure to a massive dose of roentgen rays and from protracted irradiation. Notwithstanding the fact that the roentgen effect is diminished when the radiation is distributed over a longer period, a protracted irradiation is still the preferred treatment under these conditions as the skin of the mouse recovers its resistance to a repeated irradiation more rapidly than does the tumor. By distributing the radiation over a longer period, an increase in the elective effect of the roentgen rays is obtained.

In Juul's last series of experiments, radon was substituted for roentgen rays. The results of gamma irradiation with the same product of time and intensity showed a more marked effect with the employment of a great intensity for a short time than with a small intensity for a longer period. However, ulceration of the skin occurred in 6 animals irradiated with weak intensity and in 21 animals irradiated with great intensity, therefore these results do not mean that intensive irradiation gives the best therapeutic results because the sole aim is to obtain the most favorable ratio between the effect on the normal tissues

and the effect on the tumor. The important clinical deduction from Juul's experiments is that although the higher intensity may be more effective in producing destructive action in any tissue, such as a tumor and the skin intervening between the tumor and the source of radiation, yet the greater *differential* effe cts(i.e., conservation of skin and destruction of tumor) may be obtained with prolonged irradiation.

II. EXPERIMENTAL DATA

At the Memorial Hospital two series of tests have been made to compare the production of erythema on the human skin by exposure to weak radon sources for relatively long times, and to much stronger ones for correspondingly shorter times.

The reaction used was the production of a very faint erythema, so that differences in degree could be readily detected. Two tests were made in corresponding positions on each individual, one with a strong source and the other with a weak source, the times of irradiation being adjusted so that the total dose was the same in each case. When the exposure was more than a few hours, allowance was made for the decay of the radon source.

In the first series, made by one of us in collaboration with Dr. Archie Dean in 1922, and hitherto unpublished, the radiation which was used was predominantly beta. The sources were capillary glass tubes 14 mm. long, unfiltered, used at a distance of 1 cm. from the skin. The strengths of the strong tubes varied from 80 to 150 mc., of the weak ones from 0.7 to 3.5 mc. The ratios of strengths of pairs used simultaneously on one individual varied from 30 to 150. The longest time of exposure for a weak tube was four hours, the shortest for a strong one, forty seconds. Eighteen pairs of exposures were made, the results of which are given in Table III. In no case was there a marked difference between the two reactions. In 7 cases no difference could be detected; in 6 the reaction from the weaker tube was very slightly more marked; and in 5, that from the stronger tube. The range of ratios is approximately the same for all three groups. Therefore, it is evident that, *when the total time of irradiation does not exceed a few hours*, a given quantity of beta radiation will have the same effect in producing skin erythema,

TABLE III

Production of skin erythema with equal doses of radiation of different intensities—times varying from 40 seconds to 4 hours. Source—glass radon tube, no filter. Radon-skin distance, 1 cm.; dose, 2 mc-hr.

Strong Tube	Weak Tube	Ratio	Result
mc.	mc.		
81.5	0.83	98	Reactions equally intense
123.0	1.38	89	Reactions equally intense
92.0	1.25	74	Reactions equally intense
139.0	3.50	40	Reactions equally intense
93.0	2.40	39	Reactions equally intense
115.0	3.20	35	Reactions equally intense
105.0	3.40	31	Reactions equally intense
102.0	0.69	148	More marked reaction from weaker source
106.0	0.96	110	More marked reaction from weaker source
110.0	2.05	54	More marked reaction from weaker source
148.0	3.70	40	More marked reaction from weaker source
110.0	3.10	35	More marked reaction from weaker source
108.0	3.90	28	More marked reaction from weaker source
125.0	1.10	113	More marked reaction from stronger soruce
112.0	1.25	90	More marked reaction from stronger source
96.0	1.80	53	More marked reaction from stronger source
57.5	2.00	29	More marked reaction from stronger source
54.0	4.40	13	More marked reaction from stronger source

regardless of the strength of the source, within rather wide limits.

In the second series, made by the present authors, gamma radiation was used. The sources were the same type of capillary glass tube as before, but each was enclosed in a gold tube of 0.5 mm. wall thickness. The distance was 1 cm. and the dose 250 or 225 mc-hr. The strengths of the strong tubes varied from 254 to 60 mc., of the weak ones, from 5 to 2.5 mc. The ratio of exposure times used simultaneously on one individual varied from 15 to 110, the longest exposure time being eight days, the shortest one hour. Eight pairs of exposures were made, and the results are given in Table IV. In every case the reaction from

TABLE IV

Production of skin erythema with equal doses of radiation of different intensities—times varying from 1 hour to 8 days. Source—glass radon tube, filter 0.5 mm. gold. Radon-skin distance 1 cm.; dose, 225 or 250 mc-hr.

Strong Tube	Weak Tube	Ratio	Result
mc.	mc.		
254	3.3	77	More marked effect from stronger source
224	3.5	64	More marked effect from stronger source
97	2.5	39	More marked effect from stronger source
95	3.7	26	More marked effect from stronger source
95	3.8	25	More marked effect from stronger source
97	4.4	22	More marked effect from stronger source
59	4.8	12	More marked effect from stronger source
59	5.0	12	More marked effect from stronger source

a strong tube used for a short time was definitely more marked than that from the weak tube used for a correspondingly longer time. Therefore, when the range of times used is from a few hours to a few days (in contrast to a range of from a few minutes to a few hours) a greater effect is produced on the skin by a strong source acting for a short time, than by a weaker source used for a correspondingly longer time.

This result is in accordance with the findings of other observers that if all the times used in such an experiment are short in comparison with the duration of the life cycle of the cell in question, no difference will be observed with different intensities. If, on the other hand, the duration of exposure to the radiation of low intensity is comparable to the life time of the cell, a different result may be expected.

III. GENERAL DISCUSSION

Our experiments indicate that the production of a skin erythema by roentgen rays requires a greater amount of radiant energy if the exposure be long than if it be short. They are not in accordance with the general clinical opinion, now gaining many converts, regarding the disappearance of neoplasms when treated by radium, for experience is showing that relatively long exposures to small quantities of radium are better than the short exposures of high intensity formerly given. The explanation, as we have earlier implied, probably lies in the greater differential effects on tumor than on normal tissues with longer duration and less intensity of irradiation. Canti properly suggests that in the case of the skin and of tissue cultures, the result may be a direct action on the cell and that in the case of neoplasms there may be an indirect factor playing an important part.

Another equally important distinction between normal and neoplastic tissues is their "differential recovery" after exposure to radiation. Clinical and laboratory experiments tend to substantiate the theory that normal cells recover their structure and ability to function much more quickly and more completely than do neoplastic cells whenever equal and sublethal doses of radiation are given. This fact is taken advantage of in the treatment of cancer by prolonged or fractionated irradiation.

We have long contended that the results of irradiation experiments on cells in cul-

ture or simple plants could not be applied to the treatment of such a complex tissue as cancer. The two conditions are not analogous. The growth of cells *in vitro* provides an ideal opportunity for observing the direct action of radiation on cells which are isolated from the indirect effects brought about by interference with nerve and blood supplies. It is a suitable medium as far as it goes but the experimental data obtained cannot be applied unreservedly to the treatments of tumors *in situ*. For example, in the study of the time factor, it is conceivable that the tumor bed or environmental tissue may respond more or less acutely than the tumor itself to the same intensity of radiation. Preoperative external irradiation causes marked ischemic necrosis (by acute endarteritic injuries with thrombosis) in certain bulky adenocarcinomas of the breast, at a time when other cells in the same tumor show only the earliest changes produced by the direct effects of the irradiation. An interesting experiment by Dr. Honor Fell working in Strangeways' laboratory, confirms this viewpoint. She irradiated chicks *in ovo* with roentgen rays and found that with a certain dose there was no immediate destruction of the chick at the twentieth to the twenty-fifth hour of incubation, that is, before the vascular area is formed. If, however, the same dose was given to a six-day embryo, i.e., after the blood vessels have formed, then thrombosis occurred, due to destruction of the delicate endothelium. The lethal effect in this instance was presumably brought about by indirect action. The reputed advantage of prolonged weak irradiation (within limits) over short intensive irradiation in the treatment of cancer may conceivably be due in part to these indirect effects as well as to the differential tolerance of cancer and normal tissues to radiation.

Although we have been discussing external irradiation only, i.e., selective irradiation, in which the normal tissues comprising the environment of the tumor are compared in their reactions to the malignant tumors they contain, it is probable that interstitial irradiation—even though more intense—may produce different effects according to the intensity and duration of irradiation. Radon deposited interstitially has an exponential rate of decay, less than 1 per cent remaining at the end of thirty days. The irradiation by this interstitial method is therefore continuous but with diminishing intensity. There is some question in our minds concerning the relative effectiveness of continuous irradiation by radon with an exponential diminution in intensity or by radium element interstitially with a constantly equal intensity and the same total dose.

The Time Factor and the Appearance of the Tissue Reaction

Radiologists and pathologists are thoroughly familiar with the usual delay between the date of irradiation and the appearance of radiation changes in skin and tumor. It seems that the intensity of the radiation or the time consumed in delivering the treatment does not influence appreciably the interval between exposure and the appearance of the tissue reaction. This latent period is fairly constant for different biological media such as eggs, vegetable cells and human skin. Of course when the duration of irradiation is prolonged so as to consume a great portion of the latent period, the evidence of the effect of such irradiation may be tardily presented, but in practical radiation therapy this situation seldom obtains. Laboratory experiments tend to confirm this opinion. Strangeways showed that it was practically impossible to produce an immediate lethal effect on cells *in vitro;* as much as eight hours of continuous intense irradiation was given without killing all the cells of the tissue culture. Strangeways and Hopwood found that 17,000 "e" of roentgen rays, i.e., approximately 100 erythema doses, did not immediately destroy more than a small number of cells. Spear also attempted to give so much gamma radia-

tion to a tissue culture that no cells entered mitosis; he found that the doses necessary to obtain this effect were far too great to be tolerated by the human subject. These conclusions do not apply when caustic doses of interstitial irradiation or surface exposure to the beta rays or soft roentgen rays are employed.

The Time Factor and the Acquired Radioresistance of Cancer

The duration of irradiation must be neither too long nor too short. There is an optimal time of irradiation; if the exposure is prolonged beyond this time limit, the purpose of the treatments may be defeated by the acquired radioresistance of the cancer. This immunization of the neoplasm, called "radio-vaccination" by Delbet, who first described the phenomenon in 1914, results from the administration of repeated and spaced irradiations. Hence there is progressive diminution in radiosensitivity under the influence of repeated radium and roentgen treatments. Radioresistance is not an instantaneously acquired property, but a latent property of cancer tissue. It is not easily produced by a weak dose; after the administration of a strong dose, it is not manifested immediately. The acquired radioresistance of cancer may follow a single intensive but insufficient treatment or a series of irradiations with fractionation of the dose. It is after a delay of six weeks to two months that the phenomenon becomes apparent and it attains its maximum even later. Once acquired, this radioresistance persists indefinitely. At the same time that the neoplastic tissue is becoming refractory to radium or roentgen rays, the general tissues (connective tissue, blood vessels) are rendered incapable of supporting a new treatment without great danger of radionecrosis. Prolonged light irradiation over six weeks or more may destroy the radiosensitive cells in the cancer, but permits the survival of the more radioresistant cells. In the meantime the changes in the tumor environment, such as obliterative endarteritis and marked productive fibrosis, entomb these residual cancer cells in scar tissue, a state termed "abortive fibrosis" by Ewing. Like the healed tubercle, the cancer in the midst of abortive fibrosis is inactive but capable of renewed growth. The optimal time of irradiation therefore must strike a happy medium between the short intensive dose which destroys cancer and normal tissues alike, and the prolonged feeble dose which enables the cancer in part to survive. It is philosophically unsound to speak of "acquired radioresistance" of cancer unless we consider the neoplasm as a whole. Individual cells or the descendants of these cells probably do not change their sensitivity to roentgen rays or gamma rays. The phenomenon, as we conceive of it, is the survival of those cancer cells which were originally the most radioresistant, the production of fibrosis and vascular obliterative changes in the connective tissue bed of the tumor and the consequent loss in "differential sensitivity" of cancer and normal tissues upon which successful radiation therapy depends.

SUMMARY

1. A review of the literature shows that nine authors found that alterations in the factors of time and intensity (within the limits of their experiments) had no significance in the application of a given dose. Although the work of Sievert and Forssberg is an outstanding exception, the other experiments cited were inconclusive because the ratios of time were too small.

2. By five other writers, greater biological effects with less intensity and longer duration of irradiation were noted. In most of these articles all the factors in the experiments were not sufficiently analyzed.

3. In twenty other articles, greater biological effects with higher intensity and shorter duration of irradiation were noted. These include all experiments with large ratios of time (except Sievert's) and offer a great deal of carefully accumulated evidence for this conclusion.

4. Regaud's important experiments

showing greater differential effects on tumor than on normal tissues with longer duration and less intensity of irradiation are reviewed in detail. Clinical analogies are presented in substantiation of this theory.

5. In our experiments on the production of erythema in human skin, we found that if all the times used in such an experiment are short in comparison with the duration of the life span of the cell in question, no difference will be observed with different intensities. If, on the other hand, the duration of exposure to radiation of low intensity is comparable to the life span of the cell, a different result may be expected, namely, that a greater effect is produced on the skin by a strong source acting for a short time, than by a weaker source used for a correspondingly longer time.

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DISCUSSION

DR. EUGENE PENDERGRASS, Philadelphia. I enjoyed this presentation very much, and can add nothing for I have made no experimental observations. I believe this work will be of immense value to us, particularly the statement that the greater the intensity, the greater the reaction, which is in direct opposition to the statement of Professor Regaud that lengthened intensity caused no increase in reaction.

EDITH H. QUIMBY, New York City. I wish to supplement Dr. Pack's data by a statement of some earlier work of the same type. Dr. Pack's work has been done with gamma rays, and with time intervals from a few hours to a few days. Some years ago, Dr. Dean and I performed similar experiments with radiation which was a mixture of beta and gamma rays. The strengths of our sources varied from less than 1 mc. to more than 100 mc., and our times from a few minutes to several hours. We found no difference in effect whether we used a high intensity for a short time or a low intensity for a long time. It is evident that in studying data of this sort it is essential to consider the absolute length of the exposure times as well as the ratio between them. If the longest time is short in comparison with the life cycle of the test object (in this case the cells of the human skin) then no difference would be expected between the effects of long and short exposures, with correspondingly low and high intensities. This was the case with our experiments. But when the longer times are comparable with the life cycle of the test object, as in Dr. Pack's work, then differences in the results may be expected.

DR. P. S. HENSHAW, New York City. Dr. Regaud working with Dr. Ferroux in a recent experiment has not substantiated the findings of his earlier experiment on the ram's testes. In the later work these authors compared the effects of longer and shorter exposures of roentgen rays on the rabbit testes and now say that prolonged irradiation does not produce the greatest effect, and point out that the earlier results may have been due to the trauma caused by the radium implants. However, for a relative differential effect among tissues they say that a relatively greater effect can be obtained in the germinal epithelium than in the anorectal mucosa when the exposure is prolonged.

Juul in a recent report has, in the same way, compared the relative effectiveness of long and short exposures on the skin and tumor tissues of mice. He finds that for each of these the greatest destructive action is obtained with the short intense exposures. But for a *differential effect* the tumor tissues succumb to the longer exposures while the skin is able to resist the effect. One must therefore distinguish clearly between the *relative effects* produced in tissues with longer and shorter exposures and the *relative differential effects* produced among tissues with longer and shorter exposures.

DR. MAURICE LENZ, New York City. There seems to be only a very distant connection between the work reported by Dr. Pack and that done by Dr. Regaud. Dr. Pack investigated the relationship of intensity of a clinical symptom due to a functional dilatation of blood vessels known as erythema, to radiation intensity and duration of exposure. The longest duration of exposure was much shorter than in the work of Dr. Regaud. The latter conducted a histological study on the divergence in radiosensitivity of various groups of cells exposed to the same amount of radiation in relationship to radiation intensity and duration of irradiation. I do not see how the two pieces of work can be compared.

Dr. G. FAILLA, New York City. A great many experiments of the type described by Dr. Pack have been reported in the literature over many years. The results do not agree and really should not be expected to agree. There is an underlying reason which accounts for the observed discrepancies, but which has not been taken into account in the past. Experiments have been planned with the idea of administer-

ing the same dose in a short and in a long time, to see whether the same biological effect is produced in both cases. The ratio of exposure times has been the chief concern and no attention has been paid to the duration of the exposures in relation to the life cycle of the cells irradiated.

Now we may reasonably expect the same biological effect to be produced by the same dose of radiation, when the dose is administered in such a short time in comparison to the life cycle of the cell, that the biological material may be considered to be practically stationary during this interval. Accordingly, the Bunsen-Roscoe law should hold for all exposures shorter than a certain value which is different for different biological materials.

In Dr. Pack's experiments treatment extended over a period of days which is evidently long from the point of view of the cells which are responsible for the production of skin erythema. The longer treatments, therefore, were found to be less effective. On the other hand, Mrs. Quimby has mentioned experiments in which the ratio of exposure times was much larger than in Dr. Pack's experiments and yet the same erythema was produced by the same dose, irrespective of the time of exposure. It is important to note, however, that in Mrs. Quimby's experiments, the times of exposure involved were of the order of minutes and not days.

As to the bearing of this work on radiation therapy, little can be said. In this case we are concerned with the effect on more than one tissue, and it is the differential effect which is all important. It is essential to know how the tumor tissue in any particular case reacts to short and long exposure. The results obtained by irradiating the skin under different conditions give no indication of the reaction in a tumor under the same conditions.

Dr. Pack (closing). This research was stimulated by the previous experiments of Drs. Quimby and Dean. They studied the skin reaction following irradiation with varying intensities and times of exposure lasting from a few minutes to a few hours. The results of their experiments suggested that within the time limits employed, the reaction of the skin was not influenced by variable intensities of radiation provided the total dosage was the same in the tests. We elected to conduct a series of experiments wherein the time of exposure in one test was less than the expected life of an average epidermal cell and in the other test was longer than the span of life of such a cell. Only in this way did we anticipate a difference in the skin reactions when equal doses were administered.

We selected patients for these experiments with some consideration for age, complexion and texture of skin. Patients with very dark skins were not employed. The majority of the subjects were in middle life. The difference in the quality of skin texture in male and female was of little importance, inasmuch as a control experiment was performed on each patient.

MEASUREMENT OF THE RADIATION FIELD ABOUT SOURCES OF RADIUM IN ROENTGENS AND PHOTOGRAPHICALLY

By LILLIAN E. JACOBSON
Montefiore Hospital
NEW YORK CITY

THERE is a growing need for an exact method of measuring the field about small quantities of radium at close range or the range where the desired effect is to be produced. The ideal way would seem to use the same unit as in roentgen radiation, the roentgen. Judging from the number of recent publications this problem is challenging the biophysicist's ingenuity.

It might be advisable to make a brief summary of a few of the recent works on this subject.

Glasser and Mautz[4] have described a method of measuring gamma rays in roentgens. The condenser dosimeter with a small ionization chamber varying from 1.35 c.c. to 2 c.c. was employed. The roentgens were determined by calculation after obtaining the volume of the chamber and the capacity of the system.

Kessler and Sluys[6] described an apparatus for measuring roentgens directly, under a pressure of 20 atmospheres.

Failla[2] has measured the roentgens produced in a well-defined beam of gamma rays in a standard air chamber. He then calibrated a small spherical lead and a small spherical graphite chamber against the standard air chamber using gamma rays. Failla emphasized that the comparison must be made while using gamma rays. The value when calibrated with roentgen rays is 3.8 times larger than the value obtained with the same chamber when calibrated with gamma rays.

In all the above methods the chamber is too large to measure the field at distances smaller than about 4 mm.

Stahel[8] has developed an ingenious liquid chamber. The volume of the chamber can be made as small as 2 c. mm. With this chamber he can measure the field almost at

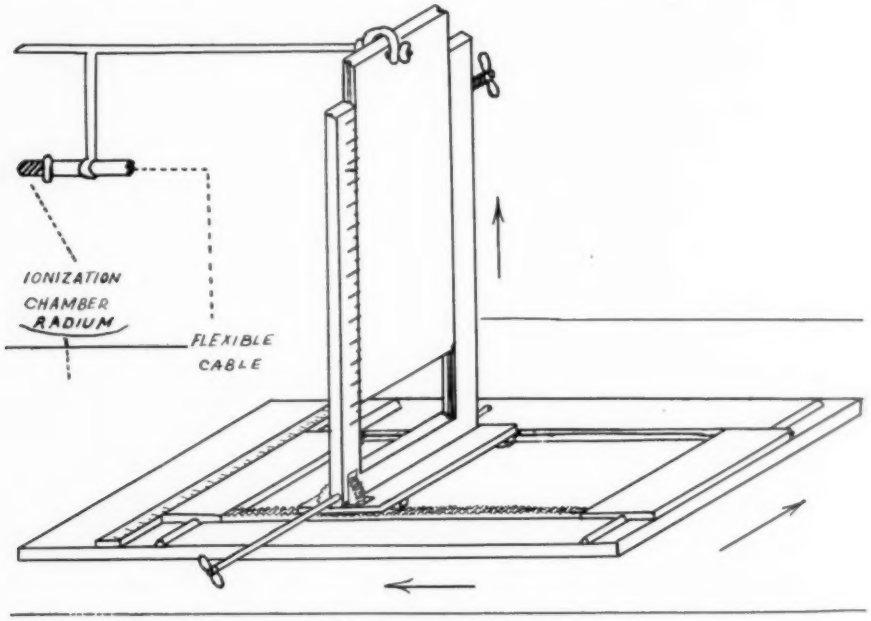


FIG. 1. Ionization chamber setup.

the surface of a radiating needle and over a very small area. He has not calibrated the chamber in roentgens, hence he has obtained only comparative measurements. But there seems no reason why the chamber cannot be calibrated in roentgens against a standard chamber if the latter calibration be correct.

Practical problems arose in the hospital which demanded solution. (1) How does the intensity change from place to place around a tube of radium? (2) How does the intensity compare at different places when the radium is concentrated, as in two radium tubes lying side by side, with that when the radium is spread out, as in two tubes end to end? (3) What percentage of the surface dose does the tumor receive in treatments with molded radium packs, and how many roentgens? (4) What is a simple method of finding the extent of the radiating field around needles used for interstitial radiation?

METHOD

The first three problems were solved by ionization measurements and photographically, the fourth photographically.

A 1 c.c. air equivalent ionization chamber attached to a Fricke-Glasser dosimeter by means of an amber flexible cable was used in making ionization measurements. An arrangement was employed whereby the chamber could be moved in three dimensions and the setting accurately repeated at any time (see Fig. 1). The radium was placed on a block of wax on the lead work bench behind 3 in. of lead. The electrometer was on another table in front of this. The leakage of the electrometer system had to be taken into account for it amounted to 5 to 10 per cent of the discharge times.

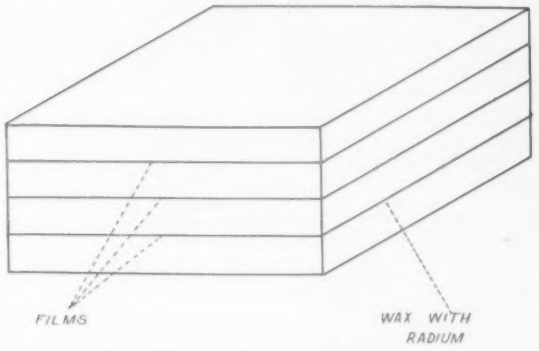


FIG. 2. Film arrangement for photographing radium.

When the field was mapped photographically the radium source was put into melted wax which covered the bottom of a lead box. A regular photographic film was cut into the desired size and wrapped again in black paper. A film was attached to each of three layers of wax 1.3 cm. thick. These were wrapped together and placed over the radium (see Fig. 2). The best exposure time was found by trial. The exposures were timed with a stop watch. The films were developed and fixed together if they were to be compared.

In mapping the radiation field about radium needles the needle was placed on

TABLE I

	r/min.			Per cent of intensity at 1.2 cm.		
Distance	Single tube	Two tubes side by side	Two tubes end to end	Single tube	Two tubes side by side	Two tubes end to end
1.2 cm.	1.00	2.04	1.61	100	100	100
1.4 cm.	0.83	1.62	1.28	83	80	80
1.7 cm.	0.61	1.18	1.06	61	58	66
2.2 cm.	0.37	0.71	0.68	37	35	42
2.7 cm.		0.47	0.47		23	29

Variation of intensity with distance in roentgens and percentage of that at 1.2 cm. of one radium tube containing 13.3 mg. radium and 1 mm. platinum filtration, two radium tubes placed side by side and two radium tubes placed end to end.

millimeter cross section paper above the film fastened to a block of wax. A hole was pricked on the line on each side of the tip, eye, and gold band (which indicates the end of the cell containing the radium salt) to show their exact position.

RESULTS

Table I shows the results of ionization measurements on one tube 1.9 cm. long and 1 mm. platinum filtration containing 13.3 mg. of radium, on two such tubes placed side by side, and on two such tubes placed end to end. The roentgen in this case is the one when the small ionization chamber is standardized for roentgen rays. According to Failla this value is 3.8 times larger than the value obtained when the chamber is standardized by comparison with the air chamber using gamma rays. Table II gives the number of roentgens obtained by using the above conversion factor.

Figure 3 shows the percentage of intensity at 1.2 cm. plotted against the distance from the center of the radium tube to the center of the ionization chamber, for one tube 13.3 mg., two tubes of 13.3 mg. each placed side by side, and two such tubes placed end to end. If the curve is extrapolated back through the 1 cm. mark the intensity is 128 per cent of that at 1.2 cm. Using this value and the number of r/min. at 1.2 cm., the calculated r/min. at 1 cm. distance from 1 gram of radium would be

TABLE II

Distance	r/min.		
	Single tube	Two tubes side by side	Two tubes end to end
1.2 cm.	0.263	0.537	0.424
1.4 cm.	0.218	0.427	0.337
1.7 cm.	0.160	0.310	0.280
2.2 cm.	0.098	0.186	0.179
2.7 cm.		0.123	0.123

Variation of intensity with distance in roentgens using Failla's factor of 3.8 of one radium tube containing 13.3 mg. radium and 1 mm. platinum filtration, two radium tubes placed side by side and two radium tubes placed end to end.

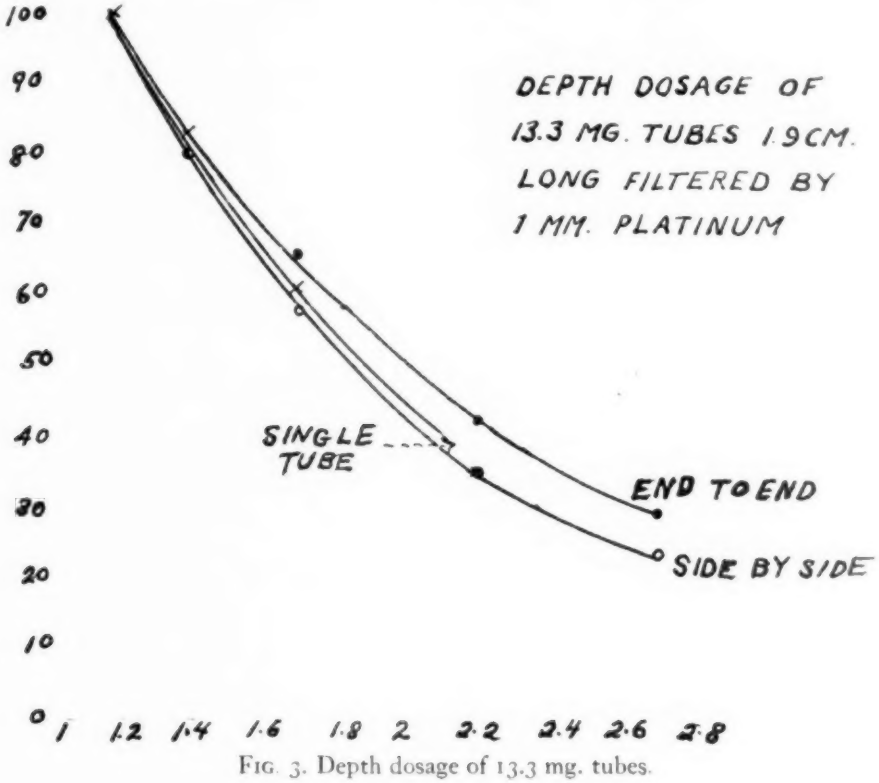


FIG. 3. Depth dosage of 13.3 mg. tubes.

25 r/min. or 28 r/min. with 0.5 mm. platinum filtration. Failla obtained 36 r/min. filtered through 2 mm. brass. If Glasser's value of 7.6 r/mg-el-hr. at 1 cm. distance is changed to r/min. and the factor 3.8 is used, the value 33 r/min. from 1 gram of radium at 1 cm. distance is obtained.

From Table 1 it is seen that the same number of roentgens are obtained at 2.7 cm. away from the tubes when the tubes are placed side by side as when placed end to end, while the number of roentgens near the tubes is greater when the radium is concentrated in the tubes side by side. Thus the depth dosage is greater with the tubes end to end, as seen in Figure 3. However the tubes were photographed and a slightly greater blackening was obtained at 2.6 cm. from the tubes when they were side by side than when they were end to end, showing that the size of the ionization chamber affects the result. But the depth dosage curves are relative curves obtained by using the same chamber and hence have reliability.

Figure 4 shows the isodose curves of a wax radium throat pack. The pack contains 77 tubes of 5 mg. each and 6 of 13.3

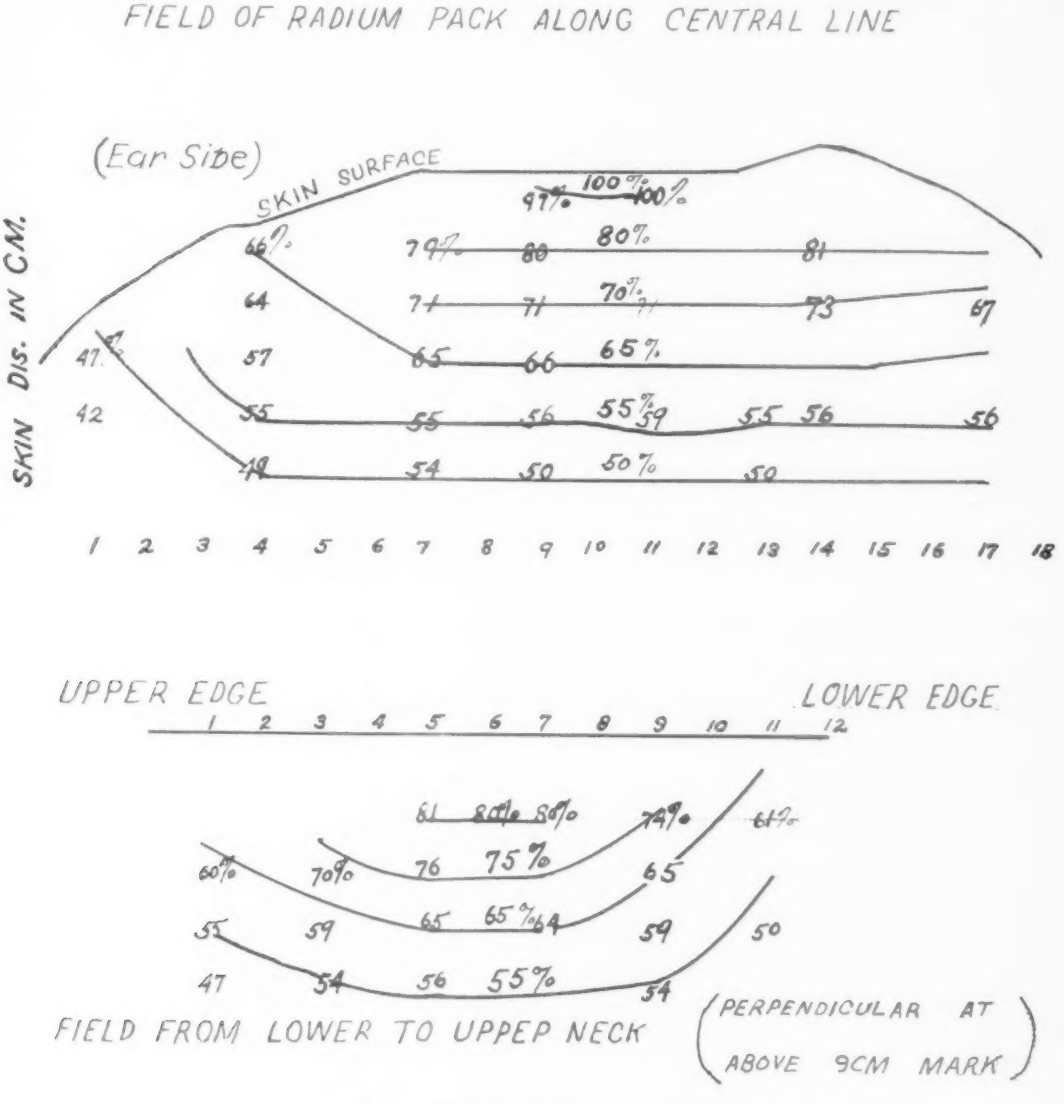

FIELD OF RADIUM PACK ALONG CENTRAL LINE
(Ear Side)
SKIN SURFACE
SKIN DIS. IN CM.
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
UPPER EDGE
LOWER EDGE
1 2 3 4 5 6 7 8 9 10 11 12
FIELD FROM LOWER TO UPPEP NECK
(PERPENDICULAR AT ABOVE 9CM MARK)

FIG. 4. Isodose curves of throat pack.

mg. each, making a total of 465 mg. The area of the pack was 140 sq. cm. The tubes were 6 cm. from the surface of the pack.

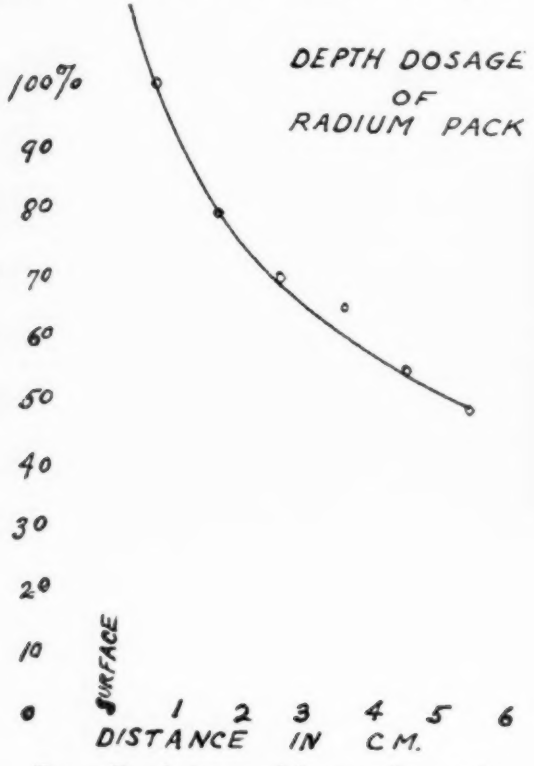


Fig. 5. Depth dosage of throat radium pack.

The 100 per cent value is 5 mm. from the surface for that is as close as one can get with the ionization chamber. The upper set of curves shows the isodose curves along a horizontal line on the neck. The lower set shows the isodose curves along a vertical line perpendicular to the horizontal line at the 9 cm. mark.

The intensity at the surface as obtained from the curves in Figure 5, which show the percentage of the intensity at 5 mm. plotted against distance from the surface, would be 113 per cent. At 4.5 cm. from the surface the intensity is 50 per cent of that at the surface. If Failla's factor of 3.8 is used, the skin receives 0.3 r/min. Since the

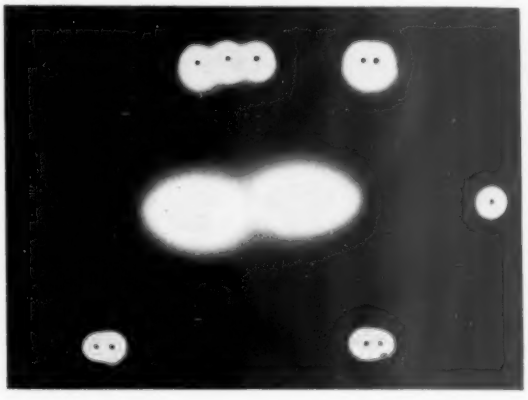


Fig. 7. Field around two 3 cm. needles with points touching.

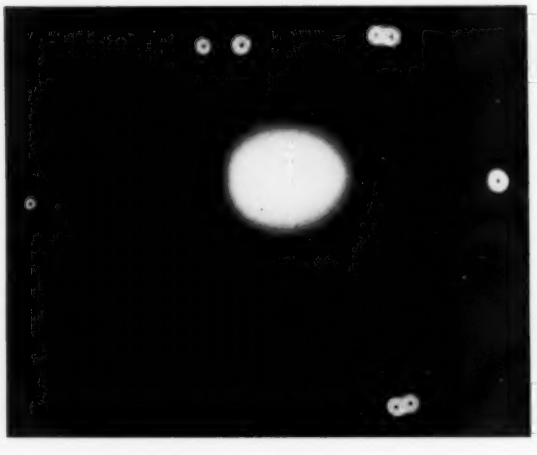


Fig. 6. Field around a 1.3 mg. radium needle 2.5 cm. long.

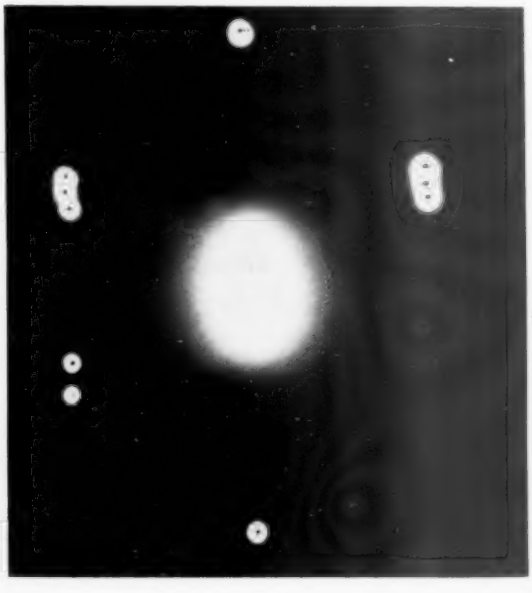


Fig. 8. Field around a 2.6 mg. radium needle 3 cm. long.

pack was used for 42,000 mg-hr. the skin received about 1,600 r and the tumor received about 800 r.

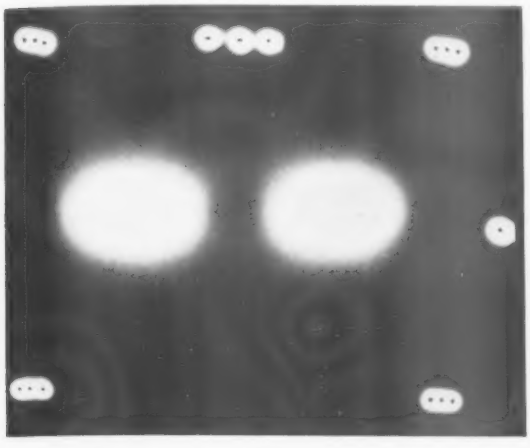


FIG. 9. Field around two 3 cm. needles with points touching.

The following paragraph is more in the nature of a gross estimate, but because of its interest I shall include it. Dr. Lenz finds that such a pack requires about 20,000 mg-hr. to produce a moderate erythema which corresponds to 780 r or 3,000 r without the conversion factor.

PHOTOGRAPHIC MEASUREMENTS

The photographs were made as described at the beginning of this paper. The exposure time was 15 min. except where noted. All the platinum needles have 0.5 mm. filtration.

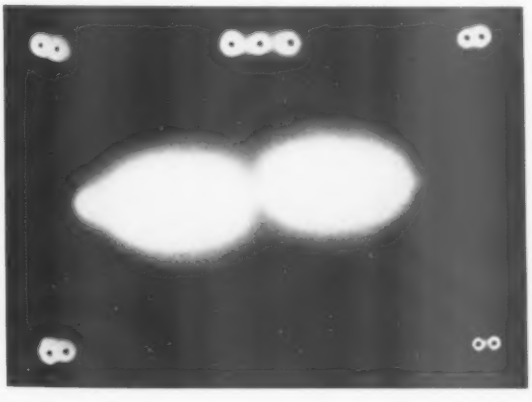


FIG. 10. Field around two 2.6 mg. radium needles 3.5 cm. long, gold bands in juxtaposition.

Figure 6 shows the field around a radium needle 2.5 cm. long containing 1.3 mg. radium. The eye end can be differentiated from the point end, for the former is pricked on both sides of the needle and the latter only on one side. Figure 7 shows two

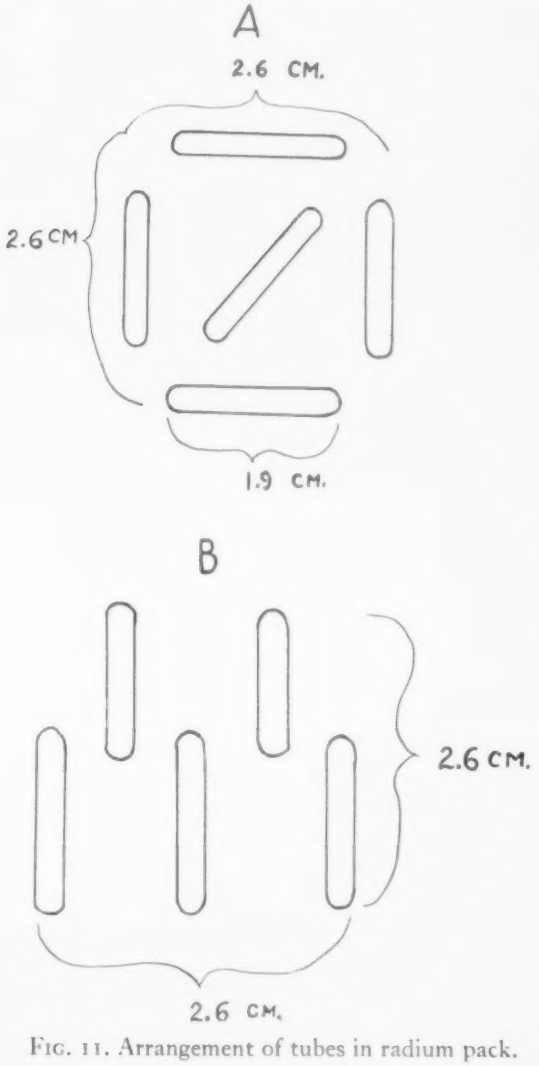
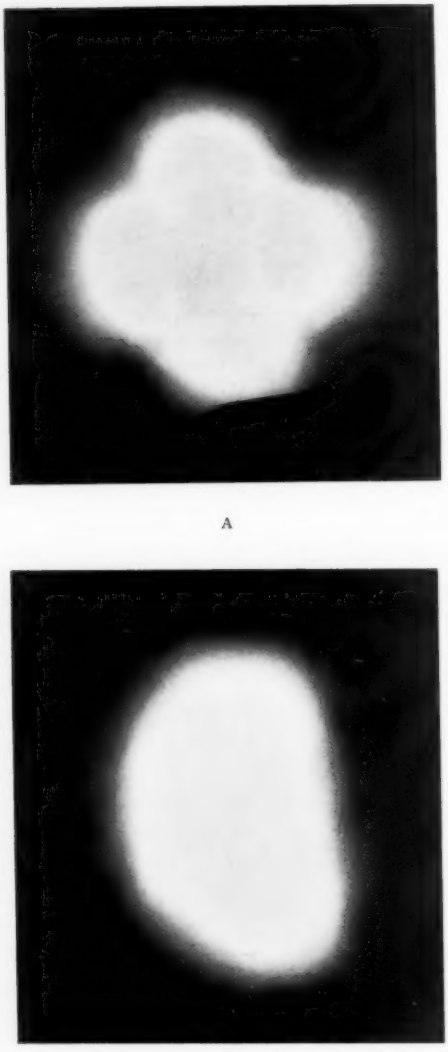


FIG. 11. Arrangement of tubes in radium pack.

such needles with gold bands in juxtaposition. The gold bands indicate the end of the radium salt container. Yet the blackening is separated by about 2 mm. Figure 8 shows the field around a radium needle 3 cm. long containing 2.6 mg. radium. Figure 9 shows two such needles with their points touching. From this figure one can find how far the radium is from the point.



A

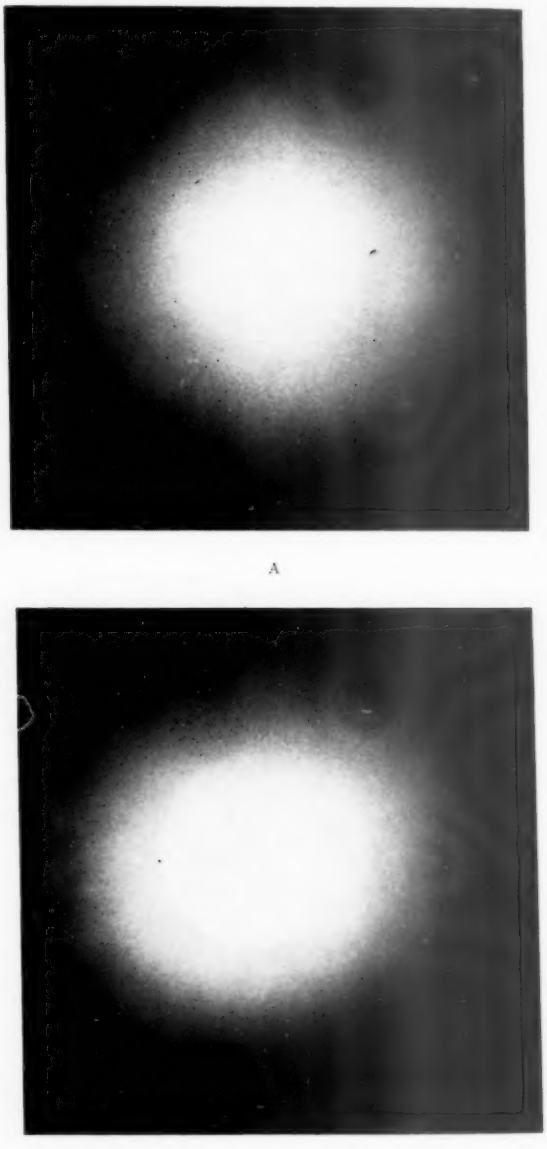
B

FIG. 12, A and B. Field in contact with radium pack.

Figure 10 shows two radium needles 3.5 cm. long each containing 2.6 mg. radium placed with gold bands in juxtaposition. The developing and fixing were exactly the same as in the case of the other needles. However, the blackening is spread over a greater area, due perhaps to the increased surface of the radiator.

Notice should also be taken of the non-uniformity of the field around one needle in Figure 10. Some of the radium salt is in a constricted portion of the needle near the eye. It thus seems advantageous to photograph the field of each needle used in order to locate irregularities.

A comparison was made between the fields of two small radium packs with the tubes arranged as in Figure 11, A and B, each containing five 5 mg. tubes. Figure 12, A and B, shows the field on the film in contact with each pack respectively. The exposure time was five minutes. Figure 13, A and B, shows the field of each respectively



A

B

FIG. 13, A and B. Field at 1.3 cm. distance from radium pack.

at a distance of 1.3 cm. Arrangement B seems to give the more uniform field.

SUMMARY

A method is given for measuring the intensity around radium tubes by ionization measurements.

The number of r/min. near several radium tubes was measured.

A comparison was made of the depth dose from radium in two tubes side by side and one long tube in the form of two tubes end to end.

Isodose curves were made on a molded wax radium pack and the intensity at the surface given in r/min.

Photographs were made of the field around radium needles and two small radium packs.

I wish to express my thanks to Dr. M. Lenz and Dr. J. Freid for their help in suggesting the problems and their interest in the investigation.

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Eighteenth Annual Meeting: Chicago, Ill., Sept., 25–30, 1933.

EDITORIALS

ROENTGEN DEMONSTRATION OF PETROSITIS

SINCE the early work of Lange and Pirie in the roentgen-ray study of mastoid disease, this method of examination has been used extensively, and from time to time various observers have added to our knowledge of the development of the mastoid and its contiguous structures, together with the types of structural development that are encountered in infancy, childhood and adult life. Notable contributions were made on this point by Gerber[1] and Bigelow[2] following Cheatle's[2] important work on the anatomical structure and development of the mastoid. With the improvements that have been made from time to time in the technical features of the examination of the mastoid, in the hands of experts the roentgen diagnosis of mastoid disease has achieved an enviable position, and since mastoid infection is among the most protean types of disease with which we are acquainted, since the clinical course and indication for surgical interference are widely varied and since each case presents a distinct problem and a distinct special study, it is essential that every bit of available information be brought to bear not only upon the anatomical structure of the mastoid but upon the extent of the disease process.

One of the severe complications associated with mastoid involvement is suppuration in the petrous portion of the temporal bone to which Profant[3] gave the name "petrositis." Since the studies of Profant, Eagleton, Kopetzky and Almour,[4] and others, regarding the anatomical, pathological and clinical characteristics of this condition, there has arisen a considerable amount of discussion as to the technique of the roentgen demonstration of petrositis. Taylor, working with Kopetzky and Almour on the roentgenographic examination of the petrous portion of the temporal bone, emphasized the difficulty of the proper demonstration of this structure owing to its inaccessibility to examination because of the overlapping of the various cranial structures. However, Taylor was able to satisfactorily demonstrate roentgenographically the petrous portions of the temporal bone and called attention to its frequent structural variations. He, among others, emphasized the necessity of a knowledge of the frequency, extent and character of its cellular development. In general, it may be said that the petrous pyramid shows a cellular development which closely parallels that of the mastoid, namely, a sclerotic petrous accompanies a sclerotic mastoid structure, while a relatively pneumatic petrous will usually be found if there is extensive pneumatization of the mastoid process, and the importance of this cannot be too strongly emphasized as the likelihood of petrous involvement seems to be directly related to its degree of pneumatization, petrositis occurring nearly always in the extensively pneumatized types. Apparently the petrous cells, as Profant says, may be involved with little or no involvement of the mastoid, and in every acute suppurative otitis media or mastoiditis the possibility of the presence and involvement of the petrous cells must be considered. Profant called attention to

[1] Gerber, Isaac. Some observations of mastoid structure as revealed by roentgen-ray examination. Am. J. Roentgenol., 1919, *6*, 1–11.

[2] Quoted by Gerber.

[3] Profant, H. J. Gradenigo's syndrome, with a consideration of "petrositis." *Arch. Otolaryngol.*, 1931, *13*, 347–378.

[4] Kopetzky, S. J., and Almour, Ralph. The suppuration of the petrous pyramid; pathology, symptomatology and surgical treatment. *Ann. Otol., Rhin. & Laryn.*, 1930, *39*, 996; 1931, *40*, 157; 396; 922.

one sign suggestive of petrositis, namely, the presence and occurrence of a profuse aural discharge in the absence of definite involvement of the mastoid or during postoperative care after a mastoidectomy. The first definite symptom to appear is pain in the area supplied by the trigeminal nerve, most commonly in the temporoparietal area.

Petrositis has been conveniently classified into three groups: first, that occurring during the course of an acute otitis media with little or no mastoid involvement; second, that which arises during an acute mastoiditis, and third, the type appearing as a postoperative sequel two or three weeks after mastoidectomy.

In a recent rather comprehensive report, Geyman and Clark[5] have called attention again to the difficulty of the roentgen technique owing to the fact that a relatively translucent bony structure must be projected through several inches of soft tissue and bone, and only by the exercise of every care and the application of all the known principles of technique can a degree of detail sufficient for diagnostic purposes be obtained. They emphasize that the technique should be simple, uniform, permit of accurate repetition, and so far as possible not be too uncomfortable for a sick patient; that the roentgenogram should show clearly the bony detail of the pyramids, give an accurate index of their relative densities, demonstrate the presence and extent of pneumatization and pathway of infection, whether antrum-epitympanic or hypotympanic. The oblique positions as described by Stenvers, Geyman and Clark found to be unsatisfactory because of the difficulty of obtaining exactly the same position and exposure on both sides. The Stenvers position, however, does show a better detail of the apices than any other position and is of value as a supplementary study. The mentovertical position, as used by Schüller, Hirtz, Grashey and Taylor, gives valuable information, but in the experience of Geyman and Clark its use on the horizontal table causes considerable discomfort to the patient and could not be consistently employed. As a substitute for this they suggest the fronto-occipital position, a position which has long been in use for the demonstration of occipital fractures as well as for the demonstration of the petrous portion of the mastoid. Worms and Bretton[6] in 1929 called attention to the advantage of this position over many of the others suggested for the examination of the petrous portion of the temporal bone. The examination is usually carried out with the patient in supine position on the horizontal table, the chin drawn in and the head slightly elevated and resting on the cassette which is placed on an angle board. The correct angle varies from 15° to 20°, depending upon the contour of the head. The central ray is perpendicular to the table and centered over the external auditory canal in the mid-sagittal line. This position shows clearly the superior portion of the pyramid. The degree and extent of the pneumatization is plainly seen for the cells follow the antrum-epitympanic route, and an index of the relative densities of the two sides is demonstrated and are easily compared because they are exposed equally on the same film.

An additional examination as suggested is one employed by Hirtz, Altschul, Grashey and others, and is called the verticomental. This position gives practically the same information as the mentovertical without the discomfort of the latter. The patient is prone on the horizontal table, the elbows flexed and the forearms and hands placed on the table in such a way as to lend support and prevent movement. The cassette is flat on the table and the chin is placed as far forward as possible. The central ray is inclined caudally enough so that it is parallel to a line from the glabella to the chin, and is centered just anterior to the external auditory meatus in the mid-sagittal line. This

[5] Geyman M. J., and Clark, D. M. The roentgen demonstration of petrositis. *Acta radiol.*, 1932, *13*, 125–133.

[6] Worms, G., and Bretton, R. L'exploration radiologique du massif pétro-mastoidien. *J. de radiol. et d'électrol.*, 1929, *13*, 23–37.

position shows the apices and adjacent structures, demonstrating apical pneumatization whether the cells follow the antrum-epitympanic or hypotympanic route and gives an excellent index as to the relative densities of the pyramids. Geyman and Clark have found that the Potter-Bucky diaphragm offers very little additional advantage over the fast screen and short exposure method.

The importance of the examination of the petrous portion of the temporal bone cannot be too strongly emphasized and a knowledge of the anatomy and structure of this bone is essential to the proper interpretation of the roentgen findings. Geyman and Clark point out the impossibility in the present state of our knowledge of an interpretation of the roentgenograms without an adequate knowledge of the clinical findings. This is due to the frequency of asymmetrical development of the mastoid structure as well as the petrous portion of the temporal bone; thus, a completely sclerotic pyramid on one side as opposed to a well pneumatized petrous on the other may only be considered evidence of disease when the clinical symptoms are consistent with such a condition. Bilateral petrositis has never been reported. Differentiation must also be made between a breakdown of intracellular structures, osteoporosis, cellularization and presence or absence of the diploic type of petrosal pyramids.

While this additional examination of the mastoid structure adds considerably both to the time and cost of the examination, it is of such essential importance that this study should not be omitted, and more familiarity with the normal variable structure that obtains in the petrous portion of the temporal bone would permit an appreciation of the pathologic changes that occur during infection.

ALFRED LEFTWICH GRAY

(1873-1932)

THERE is no structure, however strongly built, that is not affected intrinsically by the loss of one of its firmest supports, especially if that support be a component part of its foundation. Thus, today, American Roentgenology suffers a loss in the deeply regrettable death of Dr. Alfred Leftwich Gray at the acme of his professional career and at the age, almost exactly, of fifty-nine years.

Doctor Gray was born at Palmyra, Virginia, of colonial Virginian stock. His premedical education was acquired at the University of Virginia, from which he obtained also the degree of Doctor of Medicine in 1897. His ability as a teacher was recognized even before his graduation, as he became an assistant in Pathology during the course of his senior year. The teaching activities of his early post-graduate life were indicative of his versatility; at the University College of Medicine, at Richmond, he was Instructor in Anatomy and Orthopaedic Surgery from 1899 to 1901, and at the same Institution, before and after it became merged with the Medical College of Virginia, he was Professor of Physiology from 1901 to 1916. During the latter year he resigned the Professorship of Physiology to accept the Chair of Roentgenology at the Medical College of Virginia, which he occupied at the time of his death.

Doctor Gray's qualities as a medical administrator are evidenced by the fact that he was Dean of the department of Medicine at the University College of Medicine from 1909 to 1913, and, after the union of the two Schools, Dean of the School of Medicine, Medical College of Virginia until his resignation in 1920 to apply himself more actively to the teaching of Roent-

Alfred Leftwich Gray

genology alone and to his practice. The theatres of his activity in clinical Roentgenology were as numerous as had been his earlier pedagogical posts. As Roentgenologist he served faithfully, at Richmond, the Memorial Hospital, St. Luke's Hospital, the McGuire Clinic, St. Philip Hospital and Pine Camp Hospital.

His genius for organization and administration as well as his artistry in diplomacy tremendously enhanced the value of the service he gave so freely to the scientific societies in an executive capacity. At various periods in his career he had been President of the American Roentgen Ray Society, of the Medical Society of Virginia, of the Richmond Academy of Medicine and Surgery and of the American College of Roentgenology; Vice-President of the Tri-State Medical Association (the Carolinas and Virginia) and of the Southern Medical Association.

At the instant of his country's entrance into the Great War, Gray, true to his heritage of patriotism, plunged actively into the preparation for it. As a Major of the Medical Corps of the Army, he organized the Richmond School of Military

Roentgenology. Naturally, he produced officers of his own type, distinctive for efficiency and fidelity to duty. In civil life, before and after the War, his success with his students was equally great, as attested by the numbers of them that have done honor to the practice of Roentgenology, both in Virginia and beyond her boundaries. He was a painstaking teacher, forcible and convincing by methods of patience and sympathy.

Gray was never happier than when acting as host to his friends and professional colleagues and he eagerly sought opportunities to exercise every graceful act of hospitality suggested by his generous impulses—the complete personification of the ancient tradition of the South. No one of the older members of this Society, who attended it, can forget the meeting at Richmond in 1911, where it seemed that the entire medical profession, at the raising of his baton, had eagerly responded, with harmony and rhythm, in concerted welcome.

To ask counsel or help of Doctor Gray was merely to rub the Lamp of Aladdin, as discovered to his advantage and benefit by many a young radiologist, whose problem Gray regarded as his own until his wisdom evolved a solution. In matters not germane to his own field his advice was repeatedly sought—matters of general policy, of the public welfare, health and education.

His excursions into the realms of recreation were occasional, though short. He enjoyed rod and gun rather than the more usual outdoor activities of his contemporaries, but his love of Sport was for its own sake in that it involved principles of fair play and the "square deal." He was a musician of ability, both by means of the piano and the mandolin. He indulged his love for the Classics as a source of pure mental recreation. His favorite was the Latin, which he composed orally with relish and skill.

* * *

The mundane shrines of Alfred Gray's worship were those of his Nation, his State, his Hearthstone, his Calling and his Friends. His concept of these materialities transmuted them, by the alchemy of the soul, into Principles by which he lived. While he lived by them all with religious impartiality, his hobby was the fertilization of friendships. He was a veritable nurseryman of men's hearts, transfusing them with the essence of his own, hypertrophic and heavy with its infiltration of pure gold.

"Whom the Lord loveth He chasteneth," and Death met him at the end of the rough road of bodily anguish, along which he had marched for nineteen months with chin up and eyes front, seeing clearly and with complete understanding. Thus, Death ever meets the Legion of the Valiant, and always at the salute, as it swings past him into the glory of the Great West.

Percy Brown

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. E. P. Pendergrass, University Hospital, Philadelphia, Pa.
Annual Meeting: Chicago, Ill., Sept. 25–30, 1933.

American College of Radiology
Secretary, Dr. Albert Soiland, 1407 S. Hope St., Los Angeles, Calif.
Annual Meeting: Chicago, Ill., Sept. 25–30, 1933.

Section on Radiology, American Medical Association
Secretary, Dr. J. T Murphy, 421 Michigan St., Toledo, Ohio.
Annual meeting: Milwaukee, Wis., 1933.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y.
Annual Meeting: Atlantic City, N. J., Nov. 28–Dec. 2, 1932.

Radiological Section, Los Angeles County Medical Society
Secretary, Dr. D. R. MacColl, 2826 S. Hope St., Los Angeles, Calif.
Meets on the third Wednesday of each month at the California Hospital.

Radiological Section, Southern Medical Association
Secretary, Dr. C. H. Heacock, 20 S. Dunlap St., Memphis, Tenn.
Annual meeting: Birmingham, Ala., Nov. 16–18, 1932.

Brooklyn Roentgen Ray Society
Secretary, Dr. J. J. Masterson, 401-76th St., Brooklyn, N. Y.
Meets monthly on first Tuesday, October to April.

Buffalo Radiological Society
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y.
Meets second Monday of each month except during summer months, place of meeting selected by the host.

Chicago Roentgen Society
Secretary, Dr. George M. Landau, 660 Groveland Park.
Meeting second Thursday of each month October to May inclusive at Virginia Hotel.

Cincinnati Radiological Society
Secretary, Dr. H. G. Reineke, Christian R. Holmes Hospital, Cincinnati, Ohio.
Meetings held monthly.

Cleveland Radiological Society
Secretary, Dr. M. A. Thomas, Medical Arts Bldg.
Meetings are held at 6:15 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital.
Meets monthly on first Thursday from October to May, at Wayne Country Medical Society Building.

Florida Radiological Society
Secretary, Dr. W. McL. Shaw, 418 St. James Bldg., Jacksonville, Fla.
Meetings held twice a year, May and November.
Next meeting, Jacksonville, November, 1932.

Illinois Radiological Society
Secretary, Dr. L. M. Hilt, Myers Bldg., Springfield, Ill.
Regular meetings held quarterly.

Indiana Roentgen Society
Secretary, Dr. J. N. Collins, Indianapolis, Ind.
Annual meeting each February 22 in Indianapolis.

Milwaukee Roentgen Ray Society
Secretary, Dr. J. E. Habbe, 221 Wisconsin Ave., Milwaukee, Wis.
Meets first Friday in October, December, February and April.
Place of meeting designated by the president.

Minnesota Radiological Society
Secretary, Dr. L. G. Rigler, University Hospital, Minneapolis, Minn. Next meeting, Minneapolis, Minn., February, 1933.

New England Roentgen Ray Society
Secretary, Dr. Thomas R. Healy, 370 Marlboro St., Boston, Mass.
Meets monthly on third Friday, Boston Medical Library.

New York Roentgen Society
Secretary, Dr. C. W. Schwartz, 33 E. 68th St., New York City.
Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

Central New York Roentgen Ray Society
Secretary, Dr. M. T. Powers, 250 Genesee St., Utica, N. Y.
Three meetings a year—January, May and November.

Pennsylvania Radiological Society
Secretary, Dr. W. E. Reiley, Clearfield, Penna.

Philadelphia Roentgen Ray Society
Secretary, Dr. Karl Kornblum, 3400 Spruce St.
Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thomson Hall, College of Physicians, 19 S. 22d St.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Stafford L. Warren, Strong Memorial Hospital.
Meets monthly on the first Friday evening at 7:45 at the Rochester Medical Association Building.

St. Louis Roentgen Club
Secretary, Dr. W. K. Mueller, University Club Bldg.
Meets first week of each month. Time and place of meetings designated by president.

South Carolina X-Ray Society
Secretary: Dr. R. B. Taft, 105 Rutledge Ave., Charleston, S. C.
Meets at time and place of South Carolina State Medical Association. Next meeting, Spartansburg, April, 1933.

Texas Radiological Society
Secretary-Treasurer, Dr. C. P. Harris, Houston, Texas.
Meets annually one day preceding the meeting of the Texas State Medical Association.

University of Michigan Roentgen Ray Society
Secretary, Dr. C. C. Taylor, University Hospital, Ann Arbor, Mich.
Meets first and third Wednesday evening of the month from October to June, at 8 o'clock in the amphitheatre of the University Hospital.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Virginia Roentgen Ray Club
Secretary, Dr. Wright Clarkson, 205 S. Sycamore St., Petersburg, Va.
Meets annually in October.
Next meeting: Richmond, Va., October, 1932.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Luis Fariñas, Animas 110, Havana, Cuba.
Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 P.M., at 32 Welbeck St., London, W. 1., or as advertised.

Electro-Therapeutic Section of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:30 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Colin Macdonald, Lister House, 61 Collins St., Melbourne, Australia.
Meets monthly at Melbourne during the winter.

Section on Radiology, Canadian Medical Association
Secretary, Dr. A. H. Rolph, 160 St. George St., Toronto, Ont.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. P. C. Fenwick, The Hospital, Christchurch. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Allies, 134, Louvain, (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Societe de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, 11/52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent secretary, Professor Dr. Haenisch, Klopstock strasse 10, Hamburg, Germany.

Süd-und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Roentgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the Fall.

Societa Italiana Radiologia Medica
Secretary, Professor M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Maracine 30, Bucarest, Rumania.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson.
Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan. Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime.

Society of Medical Radiology of Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Society of Roentgenology
Meets first Tuesday each month, October to July.

Orient

Japan X-ray Association
c/o Orthopedic Surgery, Tokyo Imperial University.
Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike, Kyoto, Japan. Meets bi-monthly on third Sunday.

ACQUIRED RADIORESISTANCE OF TISSUES

To the Editor:

I would like to ask the help of your readers in determining a point of difficulty that must occur to all radiotherapists. The question of acquired radioresistance is one of great practical importance to all who are treating patients with radium or roentgen rays, and it would be very instructive if opinions could be elicited from the experts of America.

I think it is an accepted fact that radium or roentgen treatment arouses some peculiar tissue resistance in the area treated and to those who have to give repeated treatments it would be of great help if some data could be collected and opinions given as to the dangers of repeated irradiation.

I can find no literature dealing with this question and so far we have had to rely on our clinical experience during the last twenty years.

In our annual report of this department issued some years ago, we stressed the point that if the first treatment of skin cancer with radium was not successful, a much larger dose was required at a second treatment to produce any result.

In our department, using deep roentgen therapy and radium up to 100 milligrams dosage (we have 659 mg. of radium element at our disposal), we have given over 5000 radium treatments and over 6000 deep roentgen treatments during the last eight years.

We have kept accurate records of every case treated, with follow-up examinations, but repeated investigation has failed to give us any data on which to build any theory or act as a guide to the question of acquired resistance.

It is recognized that the skin under sunlight or ultraviolet treatment will acquire a form of immunity from damage, if the treatments are gradually increased, Nature apparently calling on the pigment of the skin to act as a protective agent. How the body tissues acquire a protection against the gamma ray or roentgen ray is still a matter of uncertainty.

I have ventured to suggest that irradiation may dislocate the electrical equilibrium of the component cells of the tissue treated, and that subsequent irradiation would meet with altered electrical conditions in the cells traversed by the rays, in the same way that wireless waves may "fade" owing to some altered condition in the atmosphere.

We have now treated a large number of cases of cancer of the breast with preoperative and postoperative deep roentgen therapy and although the treatment is spread over months, we have not found any alteration in the skin, except for bronzing.

I would like to suggest that if the following questions could be debated, some valuable information could be gained from your readers.

If radium treatment for skin cancer has proved unsuccessful, how long after the first treatment can this be repeated? In our roentgen treatments we give a "recovery" or "resting" period of one day between each application and one month between each course.

So far we have had no telangiectases appearing in our patients. What is the earliest and latest time in which these skin injuries can occur?

P. CLENNELL FENWICK

Christchurch,
New Zealand

In partial reply to Dr. Fenwick's queries, attention is directed to two editorials which have recently appeared, one in this JOURNAL (September, 1932) by Dr. A. U. Desjardins on "Causes of Cell Death in Irradiated Tissue," and the other in the *American Journal of Cancer* (September, 1932) by Dr. Francis Carter Wood on "Cell Resistance Incited by Radiation." A perusal of these two editorials will lead to a fair understanding of the changes that take place in and around tumors and of the main factors that bring about increased resistance of cells to radiation.

If other readers of the Journal have had experience at variance with the opinions expressed in these two editorials, we are quite sure that Dr. Fenwick would like to have them communicate directly with him or through the columns of the Journal. —ED.

THE APPEARANCE OF OSSIFICATION CENTERS

To the Editor:

In the excellent article on "Fractures of the Ankle" by Dr. Paul A. Bishop (this Journal, July, 1932) it is stated on page 59, "A more or less centrally located ossification center appears in roentgenograms of the tibial epiphysis at two years, according to Cohn; somewhat later, according to most anatomists, and in the fibula early in the second year."

A study of roentgenograms in young children will usually demonstrate the centers at a much earlier age; thus, with regard to the tibia, it was present in each of 7 instances during the first year (6 female and 1 male), the youngest being seven months old and the male nine months, and in every one of 4 instances in males and 5 in females in the second year, as well as in all of 11 boys and 16 girls, two years of age. Borovansky and Hnevkovsky of Prague found a center for the distal tibial epiphysis in a boy aged three months.

With regard to the fibula, of 4 instances in girls in their first year and one in a boy of nine months, the center was present on both sides in a girl aged eleven months, as well as in the boy, while of the 4 instances in boys and 5 in girls, in their second year, the center was present in every instance except in a boy aged one year and eight months, as well as in all of 11 boys and 16 girls, two years of age.

With regard to the article by Drs. Kerr and Rypins on "The Roentgen Diagnosis of Fetus Papyraceus in Utero" (July, 1932), it is stated on page 90: "In this case, the fetus papyraceus shows centers for the calcanei and sternum which would put the age between six and seven months, although the measured length is only 23 cm."

Actual roentgenological investigation shows that the center for the calcaneus appears appreciably earlier; thus in all of 5 male fetuses from 16.5 to 22.4 cm. (20 to 26 weeks) centers were present on both sides, as well as in all 10 larger specimens, while they were likewise found present in 3 female fetuses from 20.5 to 23.3 cm. (23 to 26 weeks), absent in one of 21.6 cm. (24½ weeks), and present in all of 8 larger specimens except in one instance of 28 cm. (31½ weeks).

H. Flecker

Cairns, N.Q.

DR. CRANE HONORED

Following a custom inaugurated by the University of Michigan three years ago, the choice of candidate for the honorary degree of Master of Arts was Dr. A. W. Crane of Kalamazoo. Everyone will agree the selection was the best that could have been made, one that will meet the approval of every member of the profession in this state whose good fortune it is to know Dr. Crane and his work. An alumnus of the University he has had a long and successful career and as a debtor to his profession he has honorably discharged the obligation. A pioneer roentgenologist, Dr. Crane has been highly instrumental in the development of the specialty. His written contributions have been marked with studied care. Gifted with a facility of speech that is rarely the lot even of those whose vocation is to speak from the public platform, he is always able to interest and to hold the attention of an audience. Even his extemporaneous discussions at medical meetings are masterpieces of well thought out exposition. Never does he indulge in platitudes. In a few well studied remarks he is able to elucidate a subject more or less abstruse or to add materially to the paper presented.

It is as a master of English prose that we wish particularly to commend Dr. Crane. He has a faculty, unfortunately too rare, of adding interest to any subject on which he assays to write. He possesses a scientific imagination and a mastery in the use of metaphor. His papers are characterized by simplicity and clearness as well as harmony in his choice of words, of which he has great verbal wealth. As a phrase

artist he has few equals. To select almost at random from his writings we find such expressions (referring to that part of the anatomy immediately above the diaphragm), "costal grill," "thoracic cage," "the chest—that one cavity of the body ready-made for roentgen examination," and such expressions as "spent the best years of his professional life on a medical frontier." He writes of roentgenology, "The discovery was unexampled in dramatic surprise and promise," "The miracle of shadows by invisible light gave increasing power and precision to diagnosis," "It is the part of the pioneer to brave dangers and hardships. In this far region of the spectrum were lurking unknown dangers, unseen, insidious, deadly." "Pioneers in science, like pioneers in a new country, live often at isolating distances."

As a writer of English, Dr. Crane is in the same class as such writers as Allbutt, Osler, and a handful of savants of our own land who have been distinguished for their literary as well as their scientific contributions. His is a fine craftsmanship of the pen.

To the University as well as to Dr. Crane the Journal extends its congratulations.—EDITORIAL from the *Journal of the Michigan State Medical Society*, November, 1932, *31*, 718.

MINNESOTA RADIOLOGICAL SOCIETY

The Minnesota Radiological Society held its twelfth meeting at St. Luke's Hospital, Duluth, Minnesota, on October 8, 1932. The following papers were presented: "Roentgen Findings in Pneumoconiosis" by Dr. J. R. McNutt, Duluth; "Roentgen Therapy in Carcinoma of the Uterine Corpus" by Dr. F. B. Exner, Minneapolis; "Roentgen Visualization of the Urethra, Normal and Pathological" by Dr. M. H. Nicholson, Duluth; "Atelectasis of the Lungs" by Dr. F. Hirschboeck, Duluth; Round Table Discussion on Problems of Roentgen Diagnosis and Therapy, conducted by Dr. Gage Clement, Duluth; "Diaphragmatic Hernia: A. Roentgen Aspect" by Dr. B. R. Kirklin, Rochester; "B. Surgical Aspect", by Dr. S. Harrington, Rochester. The next meeting of the Society will be held in Minneapolis in February, 1933.

AMERICAN COLLEGE OF PHYSICIANS

The American College of Physicians will hold its Seventeenth Annual Clinical Session at Montreal, Quebec, February 6–10, 1933, with headquarters at the Windsor Hotel.

Dr. Francis M. Pottenger of Monrovia, Calif., as President of the College, has charge of the program of General Sessions. Dr. Jonathan C. Meakins, Professor of Medicine and Director of the Department, McGill University Faculty of Medicine, is General Chairman of local arrangements and in charge of the program of Clinics. Mr. E. R. Loveland, Executive Secretary, 133 South 36th St., Philadelphia, Pa., is in charge of general business arrangements, and may be addressed concerning any feature of the forthcoming Session, including copies of the program.

BOOK REVIEWS

Books Received Are Acknowledged under Heading: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers as space permits.

EXPLORATION RADIOLOGIQUE DE L'APPAREIL RESPIRATOIRE. FASCICULE I AND II. Par Emile Sergent, Professeur à la Faculté de Médecine de Paris, Membre de l'Académie de Médecine, Francis Bordet, Ancien Chef de Clinique de la Faculté de Médecine de Paris, et Henri Durand, Chef du laboratoire de la Clinique de la Charité, avec la collaboration technique de J. Couvreux, Chef du laboratoire de Radiologie de la Clinique de la Charité. Cloth. Price, 350 fr. Pp. 465, with 639 illustrations. Paris: Masson et Cie, 1931.

We find this work to be not a mere atlas but a most complete and carefully executed treatise on the roentgenologic diagnosis of diseases of the chest. As stated by the authors, the subject is presented from the clinical point of view, the endeavor being to obtain an "autopsy on the living." They express regret that from the very nature of the material to be reproduced a large portion of the wealth of detail shown on chest films is unavoidably lost. This is contrasted with reproductions of gastrointestinal films in which only gross outlines are usually needed for diagnosis. To compensate for the shortcomings of reproduction of chest roentgenograms, numerous diagrams and sketches are used as well as photographs of pathologic specimens. To render the work more compact and focus attention on the area to be studied the greater number of illustrations are detailed studies of particular areas of the chest.

The work is in three major parts. Part one deals with technique of roentgen examination and discusses the value of the clinical interpretation of roentgen findings. Part two is devoted to a study of fundamentals of interpretation and a description of roentgen images of normal and of general pathologic changes. As an example of the logical and complete manner of treatment, opacities are separately discussed and illustrated under the headings "Miliary Opacities," "Flocculent Opacities," "Spherical and Oval Opacities," "Massive Opacities" and "Linear Opacities."

The third part describes in detail the roentgenologic signs in various diseases of the thoracic cage, diaphragm, mediastinum, trachea, bronchi, pleura and lungs. The description of pulmonary changes, being most important, occupies the entire second volume of about two hundred pages.

The heart and aorta are discussed only as necessary, when their images are concerned in the diseases of the respiratory apparatus.

These volumes are easily read without a profound knowledge of French due to the simple and direct language of the text. All who obtain and study them will be well rewarded for their expenditure of time and money.

E. W. HALL

A DESCRIPTIVE ATLAS OF RADIOGRAPHS: An Aid to Modern Clinical Methods. By A. P. Bertwistle, M.D., Ch.B., F.R.C.S.Ed. Second edition, revised and enlarged. Cloth. Price, $13.50. Pp. 552, with 767 illustrations. St. Louis: C. V. Mosby Company, 1932.

The author states in his introduction that this book represents in one volume an enlarged edition of his previous Descriptive Atlas of Radiographs of Bones and Joints and his Descriptive Atlas of Visceral Radiograms, together with a chapter on Radiodiagnosis and one on its progress. While he hopes that this atlas may be of service to the roentgenologist, he intends it primarily for the clinician who, without being especially concerned with the technical side, yet desires to know what roentgenology is capable of revealing to him. The practical use of the atlas, he says, does not require any special knowledge once the basic principle of roentgen diagnosis is grasped, namely, that "x-rays penetrate different media to varying extents, thus shadows of different density are cast." With the idea of its practical use for clinicians, the author has added a number of normal roentgenograms for comparison with those showing pathological conditions. The atlas readily enables the clinician to realize what types of cases are suitable for roentgen examination. He has not included rarities, unless of special interest, and has included many examples of common and important conditions in preference to curiosities.

The book will undoubtedly prove of much

value to the clinician as the author hopes. It contains 767 illustrations. An excellent detail is the practice of placing a small diagrammatic sketch opposite the roentgenogram, accurately locating the lesion. Like all atlas types of books, the text is limited.

The illustrations are grouped under the following headings: silhouette radiograph process, normal bones and epiphyses, congenital anomalies, fractures, inflammation of bones, tumors of bones, injuries and diseases of joints; a chapter each on the nasal, dental, alimentary, urinary, respiratory, nervous, vascular, thyroid and female generative systems, and muscles. Thus the entire field of roentgen diagnosis is well covered. One may well wonder, however, why scoliosis, pes cavus and planus, fragilitas ossium, osteogenesis imperfecta, osteitis deformans, osteomalacia, achondroplasia and Madelung's deformity are included in the chapter on the inflammations of bone; or why, when there is a chapter on the vascular system, an illustration depicting calcification of arteries should be included in the chapter on muscles.

As the book undoubtedly will be read by American readers, one cannot but regret that more synonyms were not used in the terminology of the various diseases: thus giant cell tumor of bone in conjunction with myeloma, or multiple cartilaginous exostoses with diaphyseal aclasis. One also regrets the omission of the possibility of detection of nonopaque foreign bodies in the lung and respiratory tract as so completely described by Manges, and the omission of illustrations of congenital syphilitic osteochondritis and infantile scurvy, all of which are of so much service to the pediatrician.

Considerable space is given to the author's method of silhouette roentgenography which consists of holding the negative to the light and tracing the margin of the skin with a mounted needle. When the negative is printed, thus outlined, the margin shows as a black line, and the background is filled with India ink. This method, he states, enables one to form an idea of what the roentgenographic findings will be when certain deformities are next encountered. It may be of interest to note that the same effect can be produced by simply coating the part with a thin barium paste before exposure. This produces, with much less effort, a similar effect in roentgenograms of the extremities, and reveals all the linear markings of the hand, sole of the foot, etc.

Throughout the text, errors in the spelling of proper names appear, evidently the result of none too careful editorial supervision. The limitation on the legends of illustrations, necessarily produced by the type of book, seems sometimes to obscure their meaning. However, all these criticisms are perhaps trivial when the size and formidable extent of the work is considered, and when one realizes how well it may serve as a ready reference book covering the entire subject of roentgen diagnosis. The book is of convenient size for reading, the print is large, and the index satisfactory, considering the rather unsystematic grouping of various diseases under the several chapter headings.

R. S. Bromer

Allgemeine und spezielle Elektrochirurgie. (General and Special Electrosurgery.) Von Dr. Med. Hans V. Seemen, Privatdozent für Chirurgie an der Universität München, Oberarzt an der Klinik Lexer. Mit einem Beitrag Elektrochirurgie der Geschwülste in Verbindung mit Strahlenbehandlung von Dr. Med. Otto Schürch, Privatdozent für Chirurgie an der Universität Zurich, Oberarzt an der Klinik Clairmont. Paper, price RM 62.00; bound, RM 66.80. Pp. 474, with 347 illustrations. Berlin: Julius Springer, 1932.

This is unquestionably one of the best books written on this subject. It is illustrated with 347 diagrams and photographs, a number of which are in color. Each illustration is accompanied by an explicit legend, so that by reading the illustrations alone one may obtain much information.

The text contains a complete reference to the work of other authors with their names in heavy type, and with the opinions expressed in a crisp manner in italics, which make the book unusually valuable for quick reference.

About one-third of the work is devoted to the physics, equipment, general principles of technique, histology of the biological effects, the preparation for operation and the postoperative treatment.

The author then devotes 235 pages to special electrosurgery in which he discusses the use of electrosurgery in aseptic operations, infected areas, inflammatory lesions, lesions of the prostrate and bladder, anal fissures, hemorrhoids, fistulae, etc. After a chapter on the treatment of benign tumors he devotes 160

pages to a discussion of the treatment of malignant tumors. He has included numerous illustrative case reports with illustrations showing the original lesion, and the successive stages in the healing process. The author has had an extensive experience over a wide field and has demonstrated his skill by remarkable results.

Dr. Schürch discusses the combined treatment of tumors by electrocoagulation with irradiation. He reports illustrative cases and has demonstrated the advantages of this combination. It would seem that this work would be valuable to every surgeon and every radiologist.

George E. Pfahler

Das Jahrhundert der Strahlen: Ein gemeinverständlicher Überblick über das Wesen und die hohe Bedeutung der verschiedenen Strahlenarten. Vortrag gehalten im Deutschen Museum zu München am 27. Mai 1929. Von Dipl.-Ing. Dr. phil. Josef Rosenthal, München. Paper. Price, RM 2.25. Pp. 29, with 18 illustrations. Leipzig: Georg Thieme, 1930.

In this little book, Dr. Rosenthal, one of the earliest roentgen-ray pioneers and an authority on radiation physics, gives a clear and highly interesting survey of the whole range of rays known at the present time. Beginning with the familiar properties of a beam of sand, water, or vapor, the author discusses the properties of cathode rays and channel rays on the one hand, and gamma rays, roentgen rays, ultraviolet rays, light rays, and heat rays, on the other hand. The position of each type of radiation in the whole spectrum is clearly illustrated. Excellent roentgen pictures demonstrate the value of this type of radiation for medicine and physics.

Otto Glasser

Books Received

Intracranial Tumours: Notes upon a Series of Two Thousand Verified Cases with Surgical-Mortality Percentages Pertaining Thereto. By Harvey Cushing, Professor of Surgery, Harvard Medical School; Surgeon-in-Chief, Peter Bent Brigham Hospital, Boston. Cloth. Price, $5.00. Pp. 150, with 111 illustrations. Springfield, Illinois; Baltimore, Maryland: Charles C Thomas, 1932.

Endocrine Medicine. By William Engelbach, M.D., F.A.C.P., B.S., M.S., D.Sc., Professor of Clinical Medicine, St. Louis University School of Medicine, 1911–1924; Physician-in-Chief, St. John's Hospital, 1909–1924; Member of Staff St. Louis, City, Jewish, Baptist Sanitarium, and Maternity Hospitals, etc. With a Foreword by Lewellys F. Barker, Professor Emeritus of Medicine, Johns Hopkins University School of Medicine. Three Volumes and an Index Volume. Cloth. Price, $35.00. Pp. 1795, with 933 illustrations. Springfield, Illinois; Baltimore, Maryland: Charles C Thomas, 1932.

Physical Therapeutic Technic. By Frank Butler Granger, A.B., M.D., Late Physician-in-Chief, Department of Physical Therapy, Boston City Hospital; Director of Physical Therapy, United States Army, etc. Revised by William D. McFee, M.D., Visiting Physician, Department of Physical Therapy, Boston City Hospital; Attending Specialist in Physical Therapy, United States Veterans' Bureau, etc. Second edition, revised. Cloth. Price, $6.50. Pp. 436, with 135 illustrations. Philadelphia and London: W. B. Saunders Company, 1932.

Classic Descriptions of Disease: With Biographical Sketches of the Authors. By Ralph H. Major, Professor of Medicine, University of Kansas School of Medicine. Cloth. Introductory price, $4.50. Pp. 630, with 130 illustrations. Springfield, Illinois; Baltimore, Maryland: Charles C Thomas, 1932.

The Cardiac Output of Man in Health and Disease. By Arthur Grollmann, Ph.D., M.D., Associate Professor of Physiology in the Medical School of the Johns Hopkins University. Cloth. Price, $4.00. Pp. 325, with 15 illustrations. Springfield, Illinois; Baltimore, Maryland: Charles C Thomas, 1932.

Tables of Cubic Crystal Structure. By I. E. Knaggs, Ph.D., and B. Karlik, Ph.D. With a Section on Alloys by C. F. Elam, M.A., D.Sc. Cloth. Price, 11/6d. Pp. 90. London: Adam Hilger, Ltd., 1932.

Handbuch der Röntgendiagnostik und -therapie im Kindesalter. Unter Mitwirkung von Fachgenossen. Herausgegeben von Prof. Dr. St. Engel, Leiter der Kinderklinik der Städt. Krankenanstalten, Dortmund, und Dr. L. Schall, Leiter der Kinderabteilung des Landeskrankenhauses, Homburg-Saar. Paper, price M. 72.00; bound, M. 75.00. Pp. 720, with 637 illustrations. Leipzig: Georg Thieme, 1933.

Röntgenstereoskopie und Zahnheilkunde. (Deutsche Zahnheilkunde, Heft 83.) Von Privatdozent Dr. J. v. Reckow, Marburg a. d. Lahn. Paper. Price, M. 6.00. Pp. 80, with 18 illustrations. Leipzig: Georg Thieme, 1933.

DEPARTMENT OF TECHNIQUE

Department Editor: Robert B. Taft, 105 Rutledge Ave., Charleston, S. C.

PARALLAX STEREOSCOPY FOR ROENTGEN RAYS*

By KENNETH S. COLE, Ph.D.

Roentgen-Ray Department of the Presbyterian Hospital
and
Department of Physiology, Columbia University

NEW YORK CITY

IN THE field of medicine, roentgen diagnosis by the roentgenoscope and stereoscopic films is playing an increasingly important part. The drawbacks to stereoscopic films are that the patient must remain in the same position while the two successive exposures are made on separate films with different positions of the tube and that the films must be viewed in a stereoscope and usually by only one person at a time. The principal improvements for stereo pictures have been in tube, film and intensifying screen advances which have shortened exposures, and in improved tube and film holders which have shortened the the time interval between exposures. The principles of the parallax method of stereoscopy have been known for some time but it has recently proved so successful for visible photography in the hands of Kanolt and Ives that it is interesting to see how well it applies for roentgen rays.

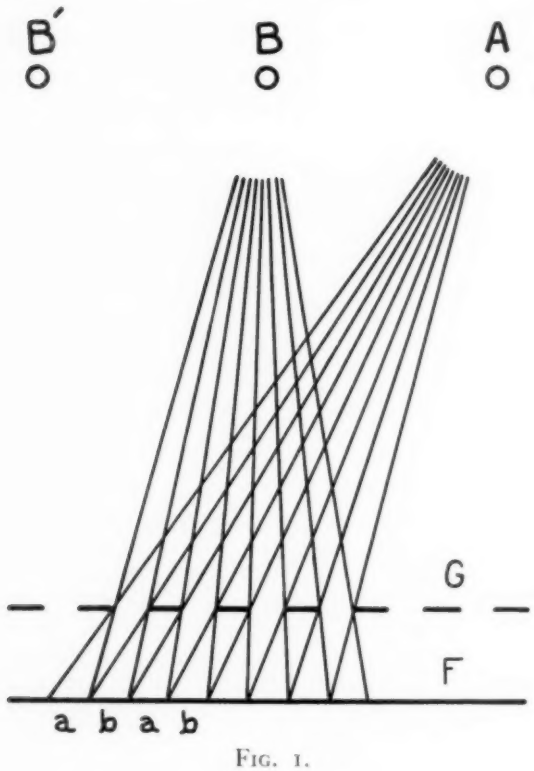

FIG. 1.

PARALLAX GRATINGS

In this method, two or more exposures are made through a grating on a single film. This exposure grating is made up of narrow strips which are alternately opaque and transparent to the rays. For the experiments reported below, the gratings were made from insulated copper wire. The wire was wound as a coil on a brass tube with adjacent turns touching. The winding was then cemented firmly together with collodion, or celluloid dissolved in acetone, and when dry it was cut along its length and removed from the tube. When this cut cylinder was unrolled into a flat sheet it was made up of straight parallel copper wires separated from each other by their insulation. The width of the opaque spaces could then be varied by the use of different sizes of wire, while various kinds of insulation gave different widths to the spaces transparent to the roentgen rays. Gratings having more than forty opaque lines to the inch have been made up by this method.

The films must be observed through a grating similar to these exposure gratings as indicated below. Since the exposure

* Presented at the Washington meeting of the American Physical Society, April 30, 1931. Abstract in *Physical Rev.*, 1931, 37, 1698.

gratings do not transmit visible light, the viewing gratings are positives made with visible light from roentgen-ray negatives of the exposure gratings.

TWO-EXPOSURE METHOD

In Figure 1 the grating *G* is made up with the opaque and transparent spaces of equal width and placed a short distance in front of the film *F*. When an exposure is made with roentgen rays from a point *A*, half of the film is exposed in narrow strips *a* through the transparent parts of the grating. The parts of the film *b* which are behind the opaque strips of the grating are still unexposed. The tube is then moved to a point *B* so that the parts of the film *a* that have been exposed from *A* are now protected from radiation from *B* by the opaque strips while the strips *b* are exposed through the transparent spaces. The film is now developed and again placed at *F* (Fig. 1), and the viewing grating replaces the exposure grating at *G*. With the object removed, an eye at *A* can see only the strips *a* and an eye at *B* can see only strips *b*. Since strips *a* and *b* show only the shadows cast by the object from points *A* and *B* respectively, then if *AB* is the interpupilary distance, both eyes give a stereoscopic effect. The shadow of the object appears in three dimensions and in its original position and size.

Exposures can be made in the manner outlined above with present equipment by the addition of the grating in the film cassette. Since the exposures are made on a single stationary film, the process can be speeded up and the effect of movement of the object largely eliminated by the use of two tubes, one at *A* and one at *B*, which are operated simultaneously. The images obtained are very sharp and with fine gratings the lines are usually not objectionable. There are a number of pairs of eye positions but only half of them give a normal effect. The other half, of which *BB'* is one, gives a pseudo-stereoscopic effect in which the image appears behind the viewing grating and film, and is reversed. Although the eye positions are somewhat limited, two or three persons can observe a film simultaneously without stereoscopes.

CONTINUOUS EXPOSURE METHODS

As the width of the opaque spaces of the gratings is increased and that of the transparent spaces decreased, it is possible to make more than two exposures on a single film. Carrying this idea further, we may use a grating having the transparent spaces about a tenth as wide as the opaque spaces and move the tube continuously during the exposure, as shown in Figure 2. The start and stop positions are so chosen that they will not overlap and expose the same strips

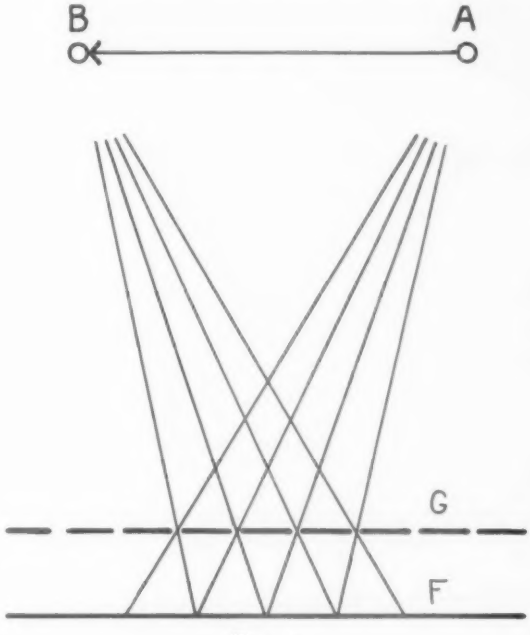

Fig. 2.

on the film twice. The developed film is then placed behind a viewing grating as before, but it can now be viewed by a number of persons over a wide angle, except at the points where it starts to repeat—or "flips." These pictures are very striking but the sharpness of the shadow decreases for the parts of the object farther from the film. This occurs because the exposed strips have an appreciable width and overlap continuously at their edges as the tube moves. It is not practical to decrease the slit width too

far because the total time of exposure will be increased to an excessive value. A very interesting possibility of the continuous picture was pointed out by Kanolt. If there are slight movements of the object during the exposure, then since the different views are taken at different times, these movements can be observed when the eyes retrace the path of the roentgen-ray tube during the exposure.

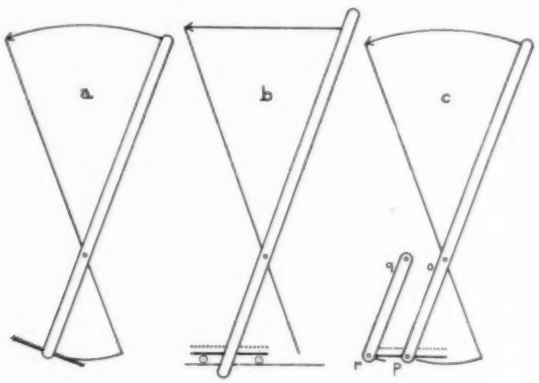

FIG. 3.

MOVING FILM METHODS

Both of the above methods have the further disadvantage that the shadow is seen either in front or in back of the film so that the eyes must focus for one distance and accommodate for another. The film and grating may be moved so as to keep the shadow of the center of the object on the same point of the film and the eyes will be better satisfied since the shadow and the film will seem to be at about the same position. This motion of the film and grating can be accomplished in several ways. As shown in Figure 3, *a*, the tube and film can be mounted on an arm which is rotated about a center in line with the center of the object. Since the film is always perpendicular to this arm it is necessary to move the grating mechanically over the film just one grating space during the complete exposure. This is analogous to the visible light photographic method devised by Kanolt. The method used in my experiments is analogous to that of Ives in which the grating is rigidly attached to but separated from the film as described above. The film with its grating and the tube move in opposite directions on parallel tracks (Fig. 3, *b*), and are controlled by sliding joints on the arm which revolves about the object as center. A third method which is shown in Figure 3, *c*, avoids the use of fine grating drives and sliding joints. The film with its spaced grating is pivoted on an arm similar to that of Figure 3, *a*. An auxiliary link *qr* of the same length as the arm between *o* and *p* and parallel to it makes the whole system like a parallel rule. The film and grating then have the desired motion as the arm is moved. Although these processes of moving the film preclude the possibility of making simultaneous exposures when applied to the two-exposure method, they have the great advantage in the continuous exposure method of sharpening the shadows of the center of the object which otherwise would have become quite fuzzy because of their distance from the film and the consequent overlapping.

FILMS AND PLATES

It has usually been possible to make the object exposures on duplitized film if the film is viewed right side up and not stretched while wet. The best results were obtained naturally with process plates and it is practically necessary to make the viewing gratings with such emulsions. It has not been possible to use intensifying screens for the continuous exposure method because of blurring.

ROENTGENOSCOPIC METHODS

The simple roentgenoscope has the disadvantage of presenting only the two dimensional shadow and this is often an inconvenient limitation. Although a stereoscopic effect was achieved shortly after the discovery of roentgen rays by means of alternate excitation of two tubes and synchronized eye shutters, the method has not been widely used. In the parallax method, an exposure grating is placed between the tube and the fluorescent screen and a viewing grating is placed between the screen and

the observer. In other words, the fluorescent screen serves as a film that can be viewed while it is being exposed. The simple two-tube method is the only one which seems promising so far. Experiments with a model using concentrated filament lamps and a translucent screen in place of roentgen-ray tubes and fluorescent screen were quite satisfactory. The advantages and limitations are the same as for the two-exposure films. With considerable surprise, it has since been found that this method is far from new, having been patented by Snook in 1904.

DISCUSSION

The fundamental difference from the visible photographic methods is that for roentgen rays we are dealing with shadows of an object in which radiation from a point source has been absorbed rather than with lens images of objects reflecting light. As a result of this the geometric relations which have been worked out by Ives apply in general by interchanging the positions of the object and the lens, substituting the point source of the radiation for the lens, and making all motions relative to the object.

It is not possible at the present time to draw any definite conclusions as to the probable usefulness of parallax methods in roentgen-ray work. They all have the advantage of recording the complete stereoscopic picture on a single film and the disadvantage of fine line shadows, but aside from these each method has its own advantages and disadvantages which can only be weighed by experience and practical requirements.

SUMMARY

In the parallax method of stereoscopy, two or more exposures are made on a single film through a grating which consists of alternate opaque and transparent lines. The developed film, when placed behind a similar grating, gives a stereoscopic effect without a stereoscope. The applications of the method for roentgen rays are analogous to those for visible light photography. Two exposures, with one or two roentgen-ray tubes, give sharp pictures with limited eye positions. Continuous exposures with a moving tube are less limited as to eye postions and their lack of sharpness can be partially overcome by a movement of the film and grating. The method is also applicable to roentgenoscopy.

REFERENCES

Snook, H. C. U. S. Patent, 758,117, 1904.
Kanolt, C. W. U. S. Patent, 1,260,682, 1918.
Ives, H. E. *J. Optic. Soc. America*, 1928, *17*, 435; 1930, *20*, 332.

PORTABLE PARAFFIN PHANTOM

By C. D. ENFIELD, M.D., *and* W. L. ABERNATHY
LOUISVILLE, KENTUCKY

A PORTABLE paraffin phantom was desired for checking surface and 10 cm. depth doses of roentgen rays on treatment installations at the office and hospital. In order to prevent the paraffin block from being damaged in transportation or when not in use, it was considered desirable to encase it in wood. In order that no difficulty or delay should be experienced in placing the Victoreen r-meter in proper relation to the phantom for the depth and surface readings, the casing was designed with a double cover so that the shallow, removable top furnishes a stand at the correct height for the insertion of the ionization chamber into the hole in the middle of the paraffin block while the deep, removable bottom section affords a rest at the proper height for placing the ionization chamber in the groove on the top of the block.

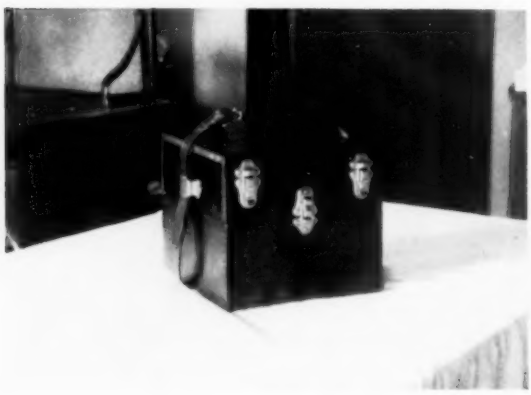

FIG. 1. Closed for transportation.

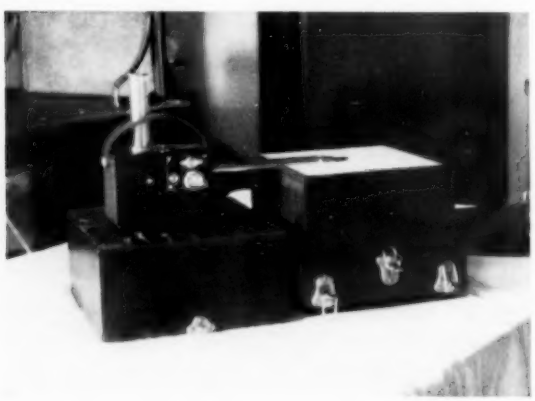

FIG. 2. In position for surface reading.

The wooden frame measures 20×20×20 cm. on the inside. A hole is bored through the casing to a depth of approximately 12 cm. so as to place the ionization chamber in the center of the block for the depth reading. A groove half as deep and of the same width as the arm which carries the ionization chamber was cut in the upper surface of the block. Standard trunk fittings and a strap were purchased at a cost of $1.50. Twenty pounds of high melting point paraffin costing $1.00 is a little more than enough to fill the casing solidly. The wooden parts are made of $\frac{3}{8}$ inch poplar.

FIG. 3. In position for depth reading.

This simple apparatus adds considerably to the convenience of checking depth and surface readings where a single Victoreen instrument and phantom have to be employed on more than one treatment installation.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

NECK AND CHEST

Wechsler, Zacharias. Die "pleuritischen" Mediastinalstreifen im Kindesalter in ihrer klinischen Bedeutung. (Pleuritic mediastinal bands in children and their clinical significance.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, July, 1931, *44*, 81–86.

Mediastinal bands are observed not infrequently in roentgenograms of children, due, according to Fanconi, to inflammatory thickening of the mediastinal pleura. They may occur (*a*) as right-sided paratracheal bands corresponding to the thickened upper posterior margin of the right lung (observed by the author in 142 instances, or 10 per cent of all roentgenograms); (*b*) as arch-shaped bands of the upper mediastinum extending partially into the field of the trachea, corresponding to both upper lung margins (in 122 instances, or 8.4 per cent), and (*c*) in rare instances as oblique right paravertebral bands corresponding to the posterior inferior margin of the right lower lobe. The bands were observed chiefly in chronic inflammatory diseases as, for example, tuberculosis of the tracheal glands. They may also occur as a result of acute pneumonic or pleuritic processes or in localized pleural effusion.—*T. Leucutia.*

Gander, G. Ein Beitrag zur Frage der verästelten Lungenverknöcherungen. (A contribution to the question of ramified lung ossification.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Oct., 1931, *44*, 448–451.

A perusal of the literature shows that 30 cases of pulmonary ossification have been described. The author adds another case in which the condition, like most of those described in the literature, was observed accidentally.

The case is that of a man sixty-eight years of age who died as the result of injuries. At the post-mortem examination an ossification of the lungs was found, the roentgenograms of the specimen revealing that this was of the ramified type. Microscopic investigations showed evidence of typical bone with regular canals and lamellar structure.

The etiology is unknown although the old age and the large amount of soot deposits which were found in the lungs in the author's case might have some significance. Simmonds who used the name of pneumopathia osteoplastica racemosa believes that the condition is second-

ary to congenital anomaly of the vessels.—*T. Leucutia.*

Käding, Kurt. Klinische Besonderheiten bei röntgenologisch tumorartigen Verschattungen der Lunge. (Clinical characteristics in tumor-like roentgen shadows of the lung.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Sept., 1931, *44*, 279–301.

Based on a study of 21 cases of primary and metastatic pulmonary tumors, a short résumé of the case reports being included in the text (with 33 illustrations), the author expresses the opinion that an accurate roentgen differentiation is not always possible. In the primary neoplasms a relative and absolute lymphopenia may sometimes be of diagnostic value, the blood pressure being somewhat lower on the side in which the tumor is localized. Several cases of inflammatory changes of the bronchopneumonic type associated with chronic tuberculosis are also described. A close cooperation of the clinician and roentgenologist is necessary in order to arrive at the correct diagnosis.—*T. Leucutia.*

Cathala, Jean, Maingot, G., and Strée. Cancer du poumon à forme d'abcès. Diagnostic differentiel radiologique des cavernes hydatique et cancéreuse. (Cancer of the lung in the form of an abscess. Differential roentgen diagnosis between hydatid cyst and cancer.) *Bull. et mém. Soc. méd. de hôp. de Par.*, May 25, 1931, *55*, 818–820.

Case report: The clinical history and physical findings of râles of bronchitis with no signs localizing the pathological process gave the impression of fibrous tuberculosis. Roentgen examination revealed a rounded, circumscribed, large mass, the center of which had a hydropneumonic appearance. The mass was located against the left chest wall a little above the diaphragm. Pulmonary markings were not changed and the hilus was normal. Hydatid cyst was considered but diagnosis of ulcerated carcinoma of the lung was made. Post-mortem examination showed a soft tumor, the center of which was half filled with milky fluid. There was no adenopathy in the mediastinum or hilus. Histologic examination revealed a primary epithelioma of the lung.

Comment: The roentgen picture on close examination shows the mass not to be regularly circular as in hydatid cyst. There is inequality of density of the wall which does not conform to a picture of a cyst. The appearance of air and fluid in the cyst occurs only after rupture into bronchus. When this occurs the cyst collapses, so that irregular softening at the center is not seen in a rounded cyst.—*Ellsworth Johnson.*

ABDOMEN

Delaigue, Albert, and Hutet, Georges. L'auscultation gastrique sous le contrôle radioscopique. (Gastric auscultation under roentgenoscopic control.) *Bull. et mém. Soc. méd. de hôp. de Par.*, May 25, 1931, *55*, 875–880.

Patients are examined in the upright or prone position by the screen and stethoscope. While digestive auscultation is not as precise as is pulmonary and cardiac, it is a method not to be neglected. One can get useful information of the filling, contraction, and emptying of the stomach. The pyloric bruit is especially instructive.—*Ellsworth Johnson.*

Ratkóczi, Nándor. Über die Ätiologie und diagnostische Bedeutung des Kaskadenmagens. (On the etiology and diagnostic significance of cascade stomach.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, May, 1931, *43*, 593–604.

Cascade stomach does not represent a subvariety of hour-glass stomach but a special change in the form and position of the stomach. The upper pouch lies high and posteriorly, while the tube-shaped antral portion extends to the right and anteriorly. One of the chief characteristics is the sudden change both in form and position. Meteorism and aerophagy must be considered only as provoking and not etiologic factors. Neither do organic lesions lead to a typical picture of cascade stomach.

It is the author's opinion that cascade stomach is produced by an active contraction of the lower gastric muscles as a result of disturbance in the balance of the antagonistic nerves of the hepatic plexus. The primary cause must be sought in adhesions or acute and chronic inflammations in the gall-bladder area. In this manner, cascade stomach represents an indirect sign of disease of the gall-bladder region. Three cases, which were confirmed at operation, are included in brief summary to support this contention.—*T. Leucutia.*

Pohlandt, Klaus. Der Ringrezessus des Bulbus duodeni als Ursache typischer Fehldiagnosen von Ulkusnischen. (The annular recess of the duodenal bulb as cause of typi-

cal erroneous diagnosis of ulcer niche.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Oct., 1931, *44*, 425–441.

Roentgenologists repeatedly diagnose as niches, conditions of the bulb which are not due to ulcers. The author found that such a condition is the anomalous projection of the annular recess of the bulb. As is known, the base of the duodenal bulb is not constituted by a plane surface but by a cardiaward concave spherical cap, which forms with the pylorus the so-called annular recess. Whenever there is a disturbed position of the longitudinal axis of the first portion of the duodenum this annular recess may project, in the second position, in such a manner that some of its mucosal folds may give the impression of a niche. A straightening out of the longitudinal axis by having the patient bend to the left (towards the examiner), and by applying deep compression will usually lead to the correct diagnosis.

The author has constructed numerous plastiline models from operative specimens and by comparing these with the roentgenograms taken previous to operation he found that the plastic modulation of the bulb is of certain aid in interpreting the roentgen images of more complicated cases.—*T. Leucutia.*

Brdiczka, I. G. Das grosse Ulcus doudeni im Röntgenbild. (The large duodenal ulcer in the roentgenogram.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Aug., 1931, *44*, 177–181.

Three cases of large duodenal ulcers (the size of a cent to a quarter) controlled at operation or autopsy are described in detail because of their unusual roentgen appearance. The more important signs were as follows: There was a rather sudden filling of the niche, a change in form or size occurring only when the position of the patient was varied. In contradistinction to the manifold picture of the barium-filled bulb, these niches remained constant and showed no peristalsis. Emptying was obtained only spontaneously with the patient on the right side. It was characteristic that the emptying always occurred very suddenly and that the filling, when the patient resumed the supine position, was just as sudden. The outline of the niche was regular, similar to that of the bulb, but there was no evidence of mucosal folds and the convergent relief of the surrounding mucosa was likewise absent. The pars superior duodeni was greatly shortened and deformed, simulating the picture of a stenosis.—*T. Leucutia.*

Melchart, Franz. Zur Frage der Fistula gastro-duodenalis in Röntgenbilde. (On the question of gastroduodenal fistula in the roentgenogram.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Sept., 1931, *44*, 335–342.

The literature is very meager on the roentgen findings of gastroduodenal fistulae. Recently, the author observed 2 cases, one of which came to autopsy. The history of both cases was somewhat similar. The symptoms dated back about thirty years. Twenty-three years later a rather sudden aggravation started which gradually led to emaciation and general weakness. Roentgen examination of the gastrointestinal tract revealed sluggish peristalsis, a very high position of the gastric outlet and a forty-eight hour residue in the caudal pole, the appearance as a whole resembling that of a tobacco pouch stomach. The post-mortem examination of one of the cases showed that the very high position of the gastric outlet was not the result of a true fistula but of an upward pull of the pyloric end of the stomach and of the duodenum from a large healed ulcer (pseudo-fistula). It is probable that a secondary inflammation of the ligamentum hepatogastricum with subsequent contraction also contributed to this cardiaward displacement of the pylorus.

In conclusion, the author briefly enumerates all reported cases of gastroduodenal fistula in which roentgen examination was made. True fistulae were described by Casella, Monroe, Haudek and Berg, while pseudo-fistulae were published by Schinz (2 cases), Hautefeuille, Löw-Beer, and the author (the above two cases).—*T. Leucutia.*

Greenwald, Harry M., and Steiner, Morris. Meckel's diverticulum in infancy and in childhood. *Am. J. Dis. Child.*, Nov., 1931, *42*, 1176–1197.

In the last two years, the authors have observed 4 cases of Meckel's diverticulum with such varied changes in the symptomatology and pathology that they thought it of value to report them and analyze all the previously reported cases in children, in an attempt to classify the various types of pathologic changes with their attending symptom-complexes. Only the cases in children up to and including the age of fifteen years were collected. Forty-seven cases were found, making a total of 51.

Three distinct types of pathologic processes causing three groups of symptom-complexes

may result when a diverticulum is present: (1) ulceration with or without perforation; (2) inflammation resulting in diverticulitis, and (3) intestinal obstruction. There are also some unusual types, not discussed in this paper, such as fecal fistulas at the umbilicus and cystic tumors, due to obliteration of the duct at both ends.

In the first group, ulceration is practically always of the peptic ulcer type and probably results from the peptic action of the secretion from heterotopic gastric mucous membranes on adjacent intestinal mucosa. In the second group (diverticulitis), the pathologic process and the symptomatology are identical with those in appendicitis. In the third group, intestinal obstruction results from the presence of the diverticulum, intussusception being the most frequent type of obstruction encountered. Another cause of intestinal obstruction occurs in cases in which the diverticulum presses against the lumen of the ileum and invaginates itself into the intestine. Still another type has been described in which bands and intussusception are not present, but coils of ileum are found wound around the diverticulum, producing a kinking of the small intestine and obstruction.

In the case reports, the authors mention the use of the fluoroscope which in one instance revealed the presence of air between the liver and the diaphragm with the patient in an upright position. In another case, a barium enema was employed which revealed during the fluroscopic examination an apparent obstruction at the hepatic flexure.

Meckel's diverticulum occurs much more frequently in males than in females. Early diagnosis in the nonperforated ulcer type is essential, since early operation results in a low mortality rate (7.6 per cent). The mortality rate in the type with perforation was 58 per cent. Patients with unexplained intestinal bleeding, particularly when it is accompanied by vague abdominal pain, should be subjected to laparotomy and a careful search made for a Meckel's diverticulum. In addition, it is emphasized by the authors that a careful search should be made for a Meckel's diverticulum, if pathologic changes are found in the appendix, insufficient to account for the symptoms that the patient may present. Radical operation, the removal of the diverticulum, is not advisable in children, if it can possibly be avoided. A search should be made for a Meckel's diverticulum in every case of intussusception, since failure to remove it may lead to a recurrence of the obstruction.—*R. S. Bromer.*

BRULE and BUSY. Cancer du pancréas à forme cachectique pure. Diagnostic radiologique. (Cancer of the pancreas in the pure cachectic form.) *Bull. et mém. Soc. méd. de hôp. de Par.*, June 8, 1931, *55*, 980–984.

A case is presented of a woman aged twenty, complaining of loss of weight. A diagnosis of cancer was made although there was no pain, icterus, or glycosuria. A mass was felt in the abdomen and marked by a leaded thread. It was then localized roentgenographically and the lead marker showed the mass to be at the second, third, and fourth portions of the duodenum. This was confirmed at operation.—*Ellsworth Johnson.*

SKELETAL SYSTEM

WEIL, MATHIEU-PIERRE, and WEISMANN-NETTER, R. Deux cas nouveaux de concrétions calcaires sous-cutanées sans sclérodermie. (Two new cases of calcareous subcutaneous concretions without scleroderma.) *Bull. et mém. Soc. méd. de hôp. de Par.*, July 20, 1931, *55*, 1449–1459.

This is a detailed report of the examination, blood chemistry and mineral metabolism studies of two cases in which calcareous concretions appeared at the menopause instead of at puberty. The appearance of these concretions was preceded by crises of acro-asphyxia. There was total absence of scleroderma, but there were disseminated telangiectases of the skin and mucous membranes.

Roentgenographically, concretions were present in the fingers and elbows. The articulations were intact. The report is illustrated by four plates and one table.—*Ellsworth Johnson.*

ACTION OF ROENTGEN RAYS AND RADIUM

ON THE

HEART AND LUNGS

EXPERIMENTAL DATA AND CLINICAL RADIOTHERAPY

BY

A. U. DESJARDINS

MAYO CLINIC

ROCHESTER, MINNESOTA

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ACTION OF ROENTGEN RAYS AND RADIUM ON THE HEART AND LUNGS

Clinical Considerations (*Continued*)

Radiotherapy for Echinococcus Cyst of the Lung. Since echinococcus cyst of the lung is generally secondary to invasion of the liver, most of the experimental and clinical evidence bearing on the effect of roentgen and radium rays on this disease will be included in the section dealing with the action of the rays on the liver. SARACENI (1925) described the case of a young girl who had suffered for some time from repeated hemoptysis, without objective pulmonary signs or clinical symptoms of tuberculosis. Roentgenologic examination of the thorax revealed, in the right superior interlobar fissure, a circumscribed and almost circular shadow which was regarded as an echinococcus cyst, because the Ghedini, Weinberg, and Casoni tests always gave a positive result. Exposure to roentgen rays at intervals of three days, through two large and opposite fields, was followed by a period of temporary improvement in general condition and symptoms, but did not have any apparent effect on the pulmonary lesion. Later, the symptoms again increased and the patient died after an unsuccessful surgical effort to deal with the condition. Saraceni was apparently justified in regarding this experience as confirming the inability of roentgen rays to influence favorably echinococcus cyst of the lung.

Radiotherapy for Pulmonary Tuberculosis. At the time that x-rays were discovered by Roentgen tuberculosis of the lungs was more prevalent than it is today. Hardly had a few months elapsed since Roentgen's first communication, when the possible therapeutic value of the rays in tuberculosis was being considered and actually put to clinical test. One of the first clinical contributions was made by ELLINGWOOD (1896), who reported two cases treated with roentgen rays by Professor H. P. Pratt. One patient was a young man aged twenty-one years, who had pulmonary tuberculosis with cavitation, cough, expectoration with bacilli, fever and weakness. Exposure of the thorax to roentgen rays was said to have been followed by distinct improvement. The condition of the other patient was reported as having shown equal improvement. In neither case was the disease regarded as cured, but the condition of both patients was rated as better than it had been for several years.

Although the experiments of LORTET and GENOUD (1896) related to the effect of roentgen irradiation on tuberculous adenitis, the positive results obtained by these early investigators encouraged others to hope that roentgen rays might prove as effective against tuberculous infection of the lungs. RENDU and DU CASTEL (1897) reported a rather remarkable case. The patient, a well-developed and vigorous young man aged twenty years, suddenly developed chills and fever and became prostrated. Two days later, the physical signs suggested pneumonic inflammation of the upper lobe of the right lung, and on the third day the local signs of pneumonia increased, but cough, expectoration and dyspnea were lacking. The maximal temperature was 39.5°C., and the pulse rate was 96, but dullness or râles could not be elicited. Ulcerative and gangrenous stomatitis of the buccal mucosa, with submaxillary lymphadenitis and cervical edema, developed. The

urine was free from albumin or blood. With slight variations the disease continued unabated for six weeks; râles became audible on the eighth day and increased rapidly during the next few days; the patient had violent chills, profuse perspiration, and daily exacerbations of fever, and his general condition deteriorated steadily. At first regarded as influenzal bronchopneumonia and later as interlobar abscess, the condition was finally diagnosed by Potain as one of caseous pneumonia. During the sixth week the patient began to expectorate, and Koch bacilli were found in the sputum. Distracted by their inability to stem the progress of the respiratory infection and influenced by the recent experiments of Lortet and Genoud, the attending physicians decided to try roentgen irradiation. After the third daily exposure, the fever began to subside and practically disappeared after the fourth exposure. Appetite and strength returned, in two weeks the patient was taken to the country, in two months he had regained thirty pounds, and the physical signs had improved correspondingly. When he was reëxamined, some time later, he was perfectly well.

Assuming that the diagnosis of acute tuberculous pneumonia was accurate, the effectiveness of irradiation parallels closely the action of the rays on other forms of pneumonia and on delayed pneumonic resolution (page 122). Since exposure to roentgen rays under clinical conditions has never been shown to have any distinct bactericidal effect, the only way in which the rays could have exerted such pronounced influence on the diseased lung would seem to have been through destruction of infiltrating leucocytes, especially lymphocytes, with resulting increase in the phagocytic and immunizing factors. The similarity in reaction to irradiation between this case and cases of delayed resolution of pneumonia reported by Musser and Edsall, Edsall and Pemberton, and others, is too striking for coincidence; the factors involved in the action of the rays must have a common basis such as that mentioned.

Bergonié and Mongour (1897) irradiated the thorax of five patients suffering from phthisis, with bacilli in the sputum, night sweats and fever, for ten minutes daily for a month or longer. In three cases the disease pursued its course uninterruptedly, the condition of one patient improved for a time, and that of the remaining patient also underwent considerable improvement, but not one was cured. A specific action on the bacilli was not perceptible, and Bergonié and Mongour concluded that, if the improvement observed in two patients was due to the rays, these must have acted on the lungs and stimulated phagocytosis. Chanteloube, Descomps and Roulliès (1897) recorded in detail the case of a young woman with rapidly progressing pulmonary tuberculosis, in whom irradiation daily or twice a day for some time was followed by distinct improvement in the condition of the lungs, but erythema of the skin, systemic reaction and anemia caused loss of weight and strength; later the appetite returned, cough diminished, the patient's condition improved considerably, and the number of bacilli decreased. Revillet (1897) mentioned the case of a young man aged eighteen years, with rapidly advancing tuberculous infection of lungs and larynx. Exposure to roentgen rays did not prevent death, but irradiation was followed by a sudden fall in temperature to 37–38°C. and diaphoresis lasting a few days, when for months previously the temperature had been steadily above 40°C. Dysphagia also abated. On interrupting irradiation for one week, fever again supervened, and when daily irradiation was resumed, the fever again diminished and the night sweats disappeared. The patient was now free from dysphagia. When an accident to the generating apparatus caused irradiation to

be again interrupted, the temperature again increased, but when the exposures were resumed, the temperature again fell below 38°C. and remained at or near this level for two weeks. In the meantime, thoracic radiodermatitis had appeared and was followed, one month later, by pain in the left side, rapid and difficult respiration, expectoration of blood-streaked sputum, deterioration of general condition, fever (40.5°C.), and the patient died. DUBARD (1898), on the contrary, failed to observe any improvement in seven patients irradiated for thirty minutes daily for an unspecified period, but since complete data were not given the reasons for his failure are not clear.

Aside from their historic interest, these documents cannot be regarded as furnishing unimpeachable evidence. Nevertheless, they indicate that the rays may have a certain effect on tuberculous lesions, without enlightening us as to their mode of action. One point must not be lost sight of. During those early days, the means of producing roentgen rays were decidedly imperfect, and the sensitiveness of different kinds of tissues was still barely suspected. Also, the significance of technique and dosage were not yet realized. In the light of these considerations, it now seems probable that if, in some cases, irradiation had not been repeated to the point of inducing radiodermatitis, the patients exposed to the rays might have derived still greater benefit, and their pulmonary lesions might have receded still more. Then, the experiments of Bergonié and Tessier (1898) and Rudis-Jicinski (1900) on the action of roentgen rays on pulmonary tuberculosis, as well as those of Lortet and Genoud (1896), Fiorentini and Luraschi (1897), Mühsam (1898), and Rodet and Bertin-Sans (1898) on tuberculosis of lymph nodes, peritoneum and other structures, apparently showed that, within certain limits, the rays exert a definite influence on tuberculous granulations and that this influence is characterized mainly by inhibited evolution of the tubercles, diminished tendency to caseation, and accelerated proliferation of connective tissue and calcification. The fact that in some experiments, such as those of Rodet and Bertin-Sans, increased tendency to repair was less pronounced than in other investigations was probably related, on the one hand, to the strain of bacilli and to the doses of culture used for inoculation and, on the other hand, to the dose of roentgen rays to which the animals were exposed as well as to the precise mode of irradiation. These different experiments, the results of which were on the whole concordant, provided a basis for further clinical application.

RUDIS-JICINSKI (1901) irradiated the thorax of twenty phthisic patients; one died, one committed suicide, and in four others the treatment did not have any perceptible effect, but in the fourteen remaining cases cough diminished or ceased, night sweats disappeared, and bacilli could no longer be found in the sputum. Of course, the patients were also kept under the best possible hygienic conditions, and it was admitted that improvement may not have been due to irradiation, but Rudis-Jicinski thought that if roentgen rays had something to do with the recovery of the patients, this was due to destruction of bacilli by the rays. BURDICK (1901 and 1902) claimed that exposure of the thorax of patients with pulmonary tuberculosis to roentgen rays was followed by decrease in temperature, cough, night sweats and diarrhea, diminished tendency to hemorrhage, increase in weight and strength and general improvement. Among others who, during this period, wrote favorably of roentgen therapy for pulmonary tuberculosis may be mentioned HAZLETON (1902),

Boido and Boido (1903), Pratt (1903), Childs (1903), Stubbert (1903), Boggs (1904), Coromilas (1904), Ransom (1904), Sandberg (1903–1904), Gruble (1904), Barnum (1905), Pancoast (1905), and Gastou (1906). Most of the reports were fairly conservative, and in the majority of cases the diagnosis had been established bacteriologically; but, as pointed out by Coomes (1903), this was not always true, and the fact that patients generally received other forms of treatment at the same time made it difficult to estimate the relative influence of irradiation. Even at this early date, Pancoast stressed the undesirable effect of too strong irradiation, a point often insufficiently realized at the present time in connection with tuberculous and other chronic inflammatory lesions in general. Such as it was, the effect of irradiation on pulmonary tuberculous processes was not sufficiently striking to induce many physicians to try it; indeed, most of those who advocated radiotherapy did not claim that this should replace other methods of treatment, but held that it was a useful adjunct to other methods and tended to hasten repair of the lesions.

Such was the status of the question when Küpferle (1913) and Küpferle and Bacmeister (1913) described their experiments on rabbits, which showed that suitable irradiation interfered with the usual evolution of tubercles, which was less advanced; central caseation was less marked, the lesions were more sharply circumscribed by connective tissue which extended toward the center, and the zone of pneumonic inflammation usually surrounding such lesions was lacking. When irradiation was started soon (one day) after inoculation, the effect on the tubercles was even greater in that the tubercles in the exposed lungs were fewer in number, small, and barely recognizable by reason of extensive connective tissue repair. As might be expected, these results were sufficiently definite to stimulate considerable interest.

De la Camp (1913) and De la Camp and Küpferle (1913) reported the results obtained by roentgen irradiation in fifteen cases of pulmonary tuberculosis. Of four cases with lesions associated with the first stage of the disease and eleven cases with lesions of the second stage, all derived some measure of benefit, while four patients with third stage lesions did not improve. Fränkel (1914–1915) recorded eighty cases, in sixty-four of which improvement in general condition, decrease in cough, disappearance of pain in the chest and of a sense of oppression, lowering of temperature, cessation of expectoration, and disappearance of bacilli from the sputum (fifty-seven cases) were thought to have been due to irradiation. Küpferle (1914–1915) reviewed his results in forty-four cases, in each of which the thorax had been exposed, through three or more fields 20 cm. sq., to doses of from 15 X to 20 X.[178] of rays filtered through 3 or 4 mm. of aluminium, two or three times a week for from two to thirty-two weeks. Nineteen patients in the first stage of tuberculosis and ten of fourteen patients in the second stage derived marked benefit, and the tuberculous lesions were regarded as clinically healed. Of the eleven patients with third-stage lesions, some improved for a short time, while others steadily became worse. Berns (1915–1916) recorded thirty cases out of a series of sixty that had been treated before the outbreak of war. The patients had been irradiated twice a week, on the average, a single dose of from 15 X to 20 X of roentgen rays then considered "hard,"[179] filtered through 3 or 4 mm. of aluminium, at a focal-skin distance of 20

[178] Kienböck units.

[179] Rays rated as between 8 and 10 on the scale of the Benoist penetrometer; such rays would now be regarded as of medium wave-length.

cm., being given at first to a field 20 sq. cm. and later 50 sq. cm., over one or two areas corresponding to the focus of pulmonary disease; later, the remainder of the affected lung also was irradiated. From eight to twenty-six exposures were made during a period of one hundred days, and the total dose varied between 250 X and 500 X. In fourteen cases the fever disappeared rapidly soon after the treatment was started; in four the temperature at the outset was normal; in five other cases irradiation had a favorable influence in spite of a normal temperature, while in the seven remaining cases exposure to the rays did not perceptibly influence an abnormally high temperature. Berns maintained that irradiation caused tuberculous granulations to be replaced by connective tissue, inferred that the rays had an indirect detoxifying effect on the tubercles, and attempted to relate the tissue changes to variations in temperature which he had observed following irradiation.

As the result of his experience in more than a thousand cases, in which ozone, climatic and hygienic conditions, medicine, diet and roentgen rays had been employed, Gibson (1915) claimed that roentgen rays were the "keystone of the arch—a true specific" against tuberculosis. He held the value of irradiation as far superior to vaccine, but did not explain why, if the rays were a true specific, other therapeutic measures should have been necessary.

Many others, among whom may be mentioned Cathcart (1917), Combe (1917), McMichael (1918), Müller (1918), Menzer (1919), Peyer (1919), Strauss (1919), Mühlmann (1920), Iselin (1920), Stephan (1921), Wilkinson (1921), Windrath (1921), Hilpert (1922), Gassul (1922–1923), De la Camp (1923), Pförringer (1923), Schulte-Tigges (1924), Le Goff (1925), Schilling (1925), Röver (1925), Hirtz (1928), Deicher and Lachmann (1928–1929), Bokay (1929), Kalvaityte (1929), and Trepiccioni and Di Natali (1931), have testified to the generally favorable influence of irradiation on tuberculosis of the lungs. Combe's experience was based on the treatment of fifty children with tuberculosis of lungs or lymph nodes. The thorax or affected region was exposed, once a week for ten weeks, to 10 H[180] of roentgen rays filtered through 3 mm. of aluminium, and the results were regarded as eminently satisfactory; but his report did not include clinical data on the individual patients. In fifteen of eighteen cases treated with roentgen rays, Müller claimed that improvement in the condition of the patients was accompanied by an increased immunity reaction and that antigen combined with exposure to the rays increased lipoid activity. Having treated twenty-nine cases (children) of tuberculosis of the hilar nodes, with or without tuberculous invasion of the lungs, by exposing large thoracic areas to from 20 per cent to 50 per cent of the human erythema dose, three, four or five times at intervals of four weeks, Bokay found that the condition of all the patients improved rapidly. Fever disappeared in two weeks, on the average. Relapse occurred in three instances, but the disease responded to a second course of treatment. Cases with advanced tuberculosis were not accepted for treatment. Menzer's experience does not appear to have been quite so satisfactory. He did not describe his method of treatment clearly, but the patients were exposed to ultraviolet rays as well as to roentgen rays, and the importance of continuing the treatment for months was stressed. Like many other authors, Mühlmann called attention to the point that roentgen therapy should be regarded strictly as an institutional method of treatment, which should not be employed in pneumonic or exudative le-

[180] Holzknecht radiochromometric units.

sions, but only in stationary or slowly progressive, indurated forms of tuberculosis. His view was that irradiation should aim to induce scarring without tissue disturbance, and he advocated a dose of from 4 X to 14 X of so-called hard rays[181] to one, two or three fields over the anterior and posterior aspect of each half of the chest. The early experience of Strauss (1919) led him to follow Fränkel's lead in using small or so-called stimulating doses; the favorable effect of roentgen irradiation surprised him and he rated the value of this therapeutic agency next to that of sunlight. Later, when he found that an insufficient quantity of radiation did not have any influence on the lesions, he employed somewhat larger doses, but continued to emphasize the danger of massive irradiation. In eleven cases treated with roentgen rays, SCHRÖDER (1921), on the contrary, was unable to observe favorable results that could not be obtained by other methods. He thought such improvement as had been noted probably had been due to other factors.

De la Camp irradiated the lungs through fields 10 cm. sq. or 10 by 15 cm., three on the right side and two on the left, and gave 0.1 H.E.D. to each field two or three times a week; gradually the dose was increased to 0.2 H.E.D. per field. All the patients were kept in hospital; if fever, catarrh, or loss of appetite supervened, the treatment was interrupted. Schulte-Tigges wrote that the majority of ninety-seven cases of pulmonary tuberculosis treated by exposure of the lungs to roentgen rays derived benefit, but the degree and duration of improvement were not specified. In three cases *Mycobacterium tuberculosis* disappeared from the sputum, while in three others the organism, which could not be demonstrated before irradiation, was found after irradiation. In the nodular type of tuberculosis a dose of 2.5 per cent to 5 per cent was advocated, while in the fibrous type a dose of 10 per cent to 30 per cent was recommended. This was to be repeated, through fields 10 cm. sq., 10 by 15 cm., or 20 cm. sq., every two weeks at first and later every three or four weeks. In all the cases of phthisis treated with roentgen rays by Le Goff, the disease was reported as having been influenced favorably, but only three case reports were given as examples. One patient apparently had so-called hilar tuberculosis. Irradiation through right and left anterior and posterior fields caused the temperature to rise for a short time; the fever then abated, cough diminished, weight and strength increased, bacilli disappeared from the sputum, and the patient was apparently cured. The second patient had tuberculosis of lungs and lymph nodes, and the material expectorated contained bacilli. After having been exposed to 500 R of rays filtered through 5 mm. of aluminium, four times at intervals of two weeks, the lymphadenitis disappeared. Alternate exposure of each half of the chest to 400 R and 600 R four times at the same intervals was attended by rapid improvement, and bacilli could no longer be found in the sputum. Other methods of treatment that may have been employed at the same time were not mentioned. Schilling also advocated small doses through many small fields and deprecated too concentrated treatment. Cases in which the disease progressed slowly or tended to become latent were considered suitable for treatment. Rest in bed, heliotherapy and tuberculin also were employed; the results were said to have been better than when roentgen rays were not used.

Others who furnished additional evidence of the favorable action of roentgen rays include ZVETKOV (1926), KOCH (1926), and VON HOLTEN (1927). GASSUL and SAND-

[181] Roentgen rays that were then rated as "hard" would now be regarded as rays of medium wave-length.

BERG (1928) found a greater tendency of the pulmonary lesions to heal, increase in weight and strength, and improvement in general condition in fifteen patients with active but slowly progressive forms of nodular or sclerotic tuberculosis of the third stage, the anterior, lateral and posterior aspects of whose thorax had been exposed to 5 per cent or 10 per cent of an erythema dose of rays generated at a potential of 180 effective kilovolts and filtered through 0.5 mm. of zinc and 3 mm. of aluminium. A total dose of 50 per cent to 100 per cent H.E.D. had been given to the different fields in from four to eight months.

Prior to 1918, roentgen rays were generally used alone or more commonly they were combined with hygienic and climatic measures the value of which had long been recognized. After 1918, an increasing number of physicians continued to use roentgen rays for local irradiation of the respiratory organs, but also employed ultraviolet rays for general irradiation, because such rays, obtained either from the sun or from artificial sources such as quartz mercury-vapor or carbon-arc lamps, had been found to exert a distinctly beneficial influence on many forms of tuberculous infection. Küpferle, Bacmeister, and De la Camp, who have been the three most prolific contributors to the literature of this subject, began to use both roentgen and ultraviolet irradiation in the treatment of their cases. Indeed, during the last few years there has been a tendency for ultraviolet rays to supersede roentgen rays in professional favor. This has probably been due to the greater availability and ease of employment of ultraviolet rays, and also to the realization that, in many tuberculous states, these rays have a distinct general tonic effect which many regard as even more valuable than the comparatively limited and local action of roentgen rays. Others have discarded or have not taken up the use of roentgen irradiation because, by itself, it cannot be relied on to cure the disease in a large proportion of cases. The majority of those who have had sufficient experience to venture an opinion have advocated roentgen therapy in the chronic, productive forms of the disease, especially during the first stage or early part of the second stage, but not in the acute and exudative forms. The method of irradiation which has had the greatest vogue has been to expose each half of the thorax through two or three fields to a small dose of rays of medium or short wave-length, and to repeat such exposure once a week for from ten to sixteen weeks, or even longer. Some have advocated irradiation through a larger number of smaller fields, while others favor larger doses at longer intervals. By all, however, the use of large or so-called tumor doses is frowned upon as less effective or actually dangerous.

MANOUKHIN (1911) contended that the body combats infection by (1) phagocytosis and by (2) leucocytolysis; the influence of the second factor was thought to be due to the appearance in the blood of special ferments which he designated as *leucocytolysins* and *antileucocytolysins*, the relative proportion or strength of which govern the number of leucocytes available to counteract the toxic influence of infectious agents. Phagocytosis was held to act in cases in which particles of India ink, dead bacteria or organisms of low virulence, or bacteria freed from toxins by washing, have been introduced into the body, while leucocytolysins enter into action when soluble albuminoid substances, such as peptone, bacterial toxins, or virulent bacteria, have found their way into the blood. He assumed that leucocytolysins are elaborated in the spleen and that the leucocytosis which follows splenectomy is due to leucocytolysins produced by removal of this organ; he maintained that leucocy-

tolysins are not destroyed by heating to 55°C., and in 1913 he claimed that small or so-called stimulating doses of roentgen rays to the spleen increase their production. He also emphasized that irradiation must be confined strictly to the spleen and that the liver should be carefully shielded from the rays, because antileucocytolysins were produced by the liver; also, that irradiation of the thyroid gland, as in exophthalmic goiter, caused leucocytolysins in the blood to decrease. Irradiation of the spleen and of the liver was regarded as having an antagonistic effect. On the assumption that small doses of roentgen rays increase the activity of cells and that the quantity of leucocytolysins can be augmented by irradiating the spleen, Manoukhin (1913) suggested the possible therapeutic advantage of splenic irradiation in pneumonia, tuberculosis and other infectious diseases. He regarded leukemia as an infection or intoxication and, in his experience, each irradiation of the spleen was followed by increase in leucocytolysins, which was greatest forty-five minutes after exposure to the rays. According to him, anything that increases leucocytolysis increases the number of polymorphonuclear leucocytes which tend to neutralize the etiologic toxin; whereupon, the size of the spleen diminishes. He admitted, however, that irradiation of the spleen also destroys leucocytes directly and that interpretation of the effects mentioned is rather difficult.

Serena (1914) tried the method in four cases of pulmonary tuberculosis and one case of tuberculous meningitis. In the last case improvement was not observed, but in three of the patients with tuberculosis of the lungs the condition improved, the fever fell with each exposure of the splenic region to 0.2 of an erythema dose of rays of medium wave length, filtered through 1 mm. of aluminium, every four or five days. Fiorini and Zironi (1915), on the contrary, were unable to confirm Serena's impression of improvement in five cases treated exclusively by splenic irradiation. Coleschi (1917) reported having treated nine cases of pulmonary tuberculosis by this method, but had not been able to trace two of them. All the patients had shown improvement for a few weeks, after which the disease had resumed its usual course. Coleschi did not give complete details concerning the technique employed, thought the transient improvement had been a psychic effect, and scouted Manoukhin's idea of increasing antibodies by killing leucocytes.

In 1921 and 1922, Manoukhin claimed to have treated more than 8,000 cases of tuberculosis, mostly of the lungs, by exposing the spleen, through one anterior and one posterior field, to about 1 Holzknecht unit of roentgen rays corresponding to 8 of the Benoist scale and filtered through 1 mm. of aluminium. Cases in the first stage of tuberculosis were irradiated once a week for eight or ten weeks, those in the second stage for twelve to fifteen weeks, and those in the third stage were exposed to two series of weekly irradiations, each series consisting of twelve to fifteen sessions, with an interval of two or three months between the two series. In first stage cases the temperature fell to the normal level, cough diminished, weight increased, harsh breath sounds disappeared, and the bronchial nodes diminished in size. In second stage cases, the disease at first appeared to be aggravated in that râles became more numerous, but later the symptoms subsided, hemorrhage and night sweats ceased, weight increased, bacilli disappeared from the sputum, and gradually roentgenographic evidence of healing of the pulmonary foci was obtained. Third stage cases were said to react much like those with second stage lesions, except that treatment had to be continued for a long time. Extreme exhaustion, chronic malarial or other

changes in the spleen, and acute infection were mentioned as contraindications. MAURIAC (1922) could not agree that increased fragility of leucocytes is essentially a defense reaction, because, when his experimental animals died from anaphylaxis or infection, the leucocytes were quite fragile for some hours before death. He contended that the regenerative power of leucocytes is a better index of the favorable effect of irradiation.

The ideas of Manoukhin did not attract many followers. VERDUN and DAUSSET (1922) also recorded striking improvement in 60 per cent of ten cases treated by weekly exposure of the spleen, through one posterior field, to 1 or 1.5 Holzknecht units of rays generated at 100 kilovolts and filtered through 3 mm. of aluminium. The diagnosis of tuberculosis had been established by the presence of bacilli in the sputum, and the patients had not received any other treatment. Fever and night sweats ceased, weight and strength increased, and cough and expectoration diminished. In the cases that had shown improvement, each irradiation had been followed by a progressive increase in the number of leucocytes to as high as 15,000 or 20,000; those cases in which improvement was most rapid had an initial polymorphonuclear leucocytosis of 80 per cent or more; the number of such cells increased, and sometimes there were twice the normal number. Verdun and Dausset naturally deduced that, in tuberculosis, leucocytosis is more important than leucocytolysis. Having found that irradiation of the spleen tends to shorten the coagulation time of blood and to arrest hemorrhage, NEDDERMEYER (1926) tried the method in six cases of pulmonary hemorrhage, with gratifying results. He thought that increased tendency of the blood to coagulate was due to destruction of blood platelets.

MICHAÏLOV (1926) reported that 80 per cent of 864 patients with productive, nodular tuberculosis of the lungs obtained substantial improvement from roentgen therapy and that, in many, clinical healing occurred; only ten patients died. Of eighty-four cases treated since 1924, whose clinical data were included in the report, eight were classed as clinically healed, six as subjectively healed, fifty-five as improved, eleven as with condition unchanged, three as worse and one as dead. The spleen and affected portions of the lungs were irradiated at the rate of one field per week for five consecutive weeks, and this was repeated after an interval of two to six weeks. The lateral splenic field included the pancreas, suprarenals and liver. In early cases, only the spleen was exposed to rays generated at 120 kilovolts and filtered through 3 mm. of aluminium.

RÉCHOU (1922) first tried Manoukhin's method in ninety-five cases of tuberculosis of the lungs; the number of erythrocytes was said to have increased considerably during the seven weeks of irradiation, the condition of all patients in whom such increase in erythrocytes occurred was said to have improved in every respect, and some were practically cured. He could not establish a definite relation between the leucocytes and the clinical features of the disease. In some cases in which improvement was noted, the number of leucocytes fell from 11,000 to 6,000, while in others the number increased to 14,000 or even to 23,720. In almost all cases Réchou noted that irradiation was followed by a considerable diminution in the number of lymphocytes. In five other cases, both the spleen and lungs were exposed to similar doses of rays, but the results were essentially the same. MUSANTE (1922) treated some patients by exposing the lungs, and others by exposing the spleen, to small doses; he found that the polymorphonuclear cells returned to normal in twenty-four hours.

Splenic irradiation, on the contrary, was always followed by leucopenia, with increase in alexins and antibodies.

Trémolières and Colombier (1922) adopted Manoukhin's basic idea but modified the technique. In twenty-three cases of advanced phthisis, usually with cavitation, they exposed the spleen, sternum and long bones to 0.9 H.E.D. of rays generated at 110 kilovolts maximum[182] and filtered through 1 mm., 2 mm., or 3 mm. of aluminium. The patients were able to lie on the right side and the beam of rays was directed obliquely through the center of the spleen so as to include the sternal region but to avoid exposing the mediastinal nodes. This was repeated once a week until the patients had been exposed fifteen or sixteen times. At first, the procedure was based on the assumption that small doses of roentgen rays to the spleen and the marrow of the sternum and long bones increased the defensive properties of the blood by acting on the iron metabolism and activating the formation of hemoglobin. Later, Trémolières, Colombier and Aris (1923) claimed that such irradiation increased the number of leucocytes and ferments, that leucocytes acted by phagocytosis and by elaborating antibodies and ferments which are liberated when the leucocytes are destroyed. Sixteen patients, who had had a full course of treatment, derived considerable benefit; fever diminished, cough and night sweats disappeared, weight and strength increased. At the beginning, the number of bacilli in the sputum increased until the fifth or sixth exposure, after which it diminished steadily. Also, the initial leucopenia was subsequently replaced by leucocytosis. In cases treated by this method they always found the number of erythrocytes increased, but never saw abnormal forms. In cases that improved irradiation also induced leucocytosis, usually marked and affecting especially the lymphocytes and eosinophiles, but leucocytosis often was preceded by leucopenia for four or five hours. Alterations in physical signs or roentgenologic features were not described, and case reports were not included.

Impelled by the favorable effect of heliotherapy and phototherapy for tuberculosis of the skin and subcutaneous tissues, Maragliano (1925) conceived the idea of exposing the entire body of patients suffering from pulmonary tuberculosis to a small dose of soft roentgen rays generated at a potential equivalent to a spark-gap of 15 cm., and filtered through 1 mm. of aluminium. The plan was to give 0.1 Holzknecht daily for ten days and to repeat after an interval of from ten to fourteen days. All the patients treated had advanced tuberculosis; the progress of the disease appeared to be retarded or arrested for a time, but real improvement was not observed. Later, Maragliano (1926) expressed the opinion that the method could not be regarded as a practical therapeutic measure.

On reviewing the clinical evidence, one is impressed by the small number of cases on which many of the foregoing reports have been based; a considerable number of these reports cannot be said to be of much value as evidence. But allowing for the fact that a certain proportion of claims have undoubtedly been overstated, some were made by men of wide experience in the field of tuberculosis and cannot be entirely discredited. The fact that others have not been able to obtain the same favorable results does not necessarily mean that their observations must have been more accurate; it is quite as likely that their failure may have been due to technical or other errors. Schröder, for example, did not observe, in the cases irradiated by

[182] Effective voltage, 78,000 volts.

him, any improvement which could not be accounted for on grounds other than irradiation; yet his observations may not be more conclusive than those of others. At least, there is no sound reason why such negative reports should receive more credit than the larger number of positive reports from workers of equal or greater experience. On the whole, the clinical observations relating to pulmonary tuberculosis agree fairly well with those relating to tuberculosis of lymph nodes and other structures. It is true that the action of roentgen rays on tuberculous lymphadenitis has been demonstrated rather more conclusively than on tuberculosis of the lungs and that roentgen therapy for the former has been generally accepted by the profession as the therapeutic method of choice. Several reasons may explain why the same method for pulmonary tuberculosis has not received such wide recognition: the experimental and clinical evidence is not so conclusive; the treatment of pulmonary tuberculosis is more generally carried out in institutions; the multiplicity of explanations for the effects observed and reported has tended to create confusion and doubt. One reason why the influence of the rays on pulmonary tuberculosis may not be so great as on tuberculosis of lymph nodes probably is that in the lungs tubercles are more numerous than those in the nodes, and greater variation in degree of evolution of the tubercles is to be found in the lungs than in the nodes. The difference in structure between the lungs and lymph nodes also may be an important element in the problem. The majority of those who have written on the subject have accepted the principles laid down by Küpferle and Bacmeister, i.e.: radiotherapy should be limited to institutions in which the condition of patients can be kept under regular observation by experts; it should be used in conjunction with other methods of recognized value and should be applied only to patients with stationary or slowly progressive forms of tuberculosis, especially during the early stage when leucocytic infiltration is likely to be most pronounced and caseation and connective tissue repair have not proceeded too far. A few have ventured to try the treatment in the more active, exudate forms of tuberculosis, but their experience was limited to a small number of cases, and they have not had many emulators.

Heilbronn (1921) and a number of others have expressed themselves as opposed to roentgen-ray treatment. Heilbronn, for example, took the ground that roentgen rays cause caseated lymph nodes to break down and that, if this should occur in the mediastinum and the nodes should rupture into the air passages, aspiration of tubercle bacilli could not be avoided. He also stressed damage of blood vessels by the rays. It is clear that Heilbronn's statements were not based on personal experience, but on vague fears for which little experimental or clinical support can be found. Ordinary therapeutic doses of roentgen rays, and especially the relatively small doses advocated for tuberculous lesions, cannot induce disturbances such as those mentioned. If they occur, they cannot be ascribed to irradiation but must be attributed to natural evolution of the disease. Others have made much of the difficulty of roentgen-ray treatment—a difficulty which can exist only for those who are unfamiliar with the technical aspects of radiation therapy. It is quite true that for the general practitioner or other physician not trained in roentgen therapy to attempt such treatment must be fraught with difficulty. As Von Hayek (1920) pointed out, roentgen therapy for pulmonary tuberculosis should be undertaken only by experienced radiologists, preferably collaborating with expert phthisiologists.

The action of roentgen rays has been explained in what may appear to be many

different ways, but it is noteworthy that nearly all such explanations are grounded on destruction or intervention of leucocytes. Some have thought that resolution of the tubercles was brought about by leucocytes, because they had found the number of leucocytes increased at some time after irradiation. For Manoukhin, the primary effect of the rays was to cause the spleen to elaborate leucocytolysins which caused the leucocytes to disintegrate and to liberate their antibodies in the blood stream. In an exhaustive consideration of the problem, FRÄNKEL (1918) drew attention to the comparative infrequency of tuberculosis of the spleen, which he attributed to the exceptional ability of the spleen to destroy bacteria and to its great immunizing power. He related the swelling of the organ in the course of infections to its importance as a source of antibodies. He added that recession and absorption of caseous material cannot be accomplished by autolysis and scarring alone, but that destruction of infiltrating leucocytes by the rays may liberate enzymes and antitoxins; this may lead to focal reaction with excretion and resorption of the caseous material. The lipolytic influence and radiosensitiveness of lymphocytes also were related to destruction of the bacilli, which was thought to result from the joint action of ferments and phagocytes. From these premises Fränkel held that the aim of radiotherapy in tuberculosis should be to increase the number of lymphocytes, that this could best be achieved by small or so-called stimulating doses to the spleen, and that large doses are dangerous. Having found a progressive increase in the number of leucocytes when irradiation was followed by improvement in the condition of patients, Verdun and Dausset inferred that the effect of the rays on tuberculosis was achieved through leucocytosis. STEPHAN (1922) claimed to have proved that small doses of radiation increase the normal activity of cells, that results in tuberculosis could be obtained only in this way, and that large doses could only damage the tissues. He claimed that radiosensitive lymphocytes form only a small part of the tubercles, and that the greater proportion of such lesions is connective tissue, which is resistant to irradiation. According to him, the important part of the defense mechanism against tuberculosis is the histiocyte, or epithelioid cell, which must be preserved and stimulated; and this was to be achieved by adopting a uniform tuberculosis dose of 20 per cent to 40 per cent of the skin unit dose, or 8 to 10 *e* units.

To analyze these various contentions it is necessary, first of all, to consider the established experimental facts. The exceptional radiosensitiveness of lymphocytes, and to a slightly less pronounced degree of polymorphonuclear leucocytes, has been proved beyond all doubt. It has likewise been convincingly shown that epithelioid cells play an important part in the late stage of lymphocytic destruction or early stage of regeneration after irradiation of the spleen, lymph nodes and other aggregations of lymphoid tissue. The exact significance of these epithelioid cells in relation to radiation effect is not well understood. It is doubtful if their appearance in slightly increased numbers three or four days after irradiation, when destruction of lymphocytes has about run its course, means that the epithelioid cells have been directly stirred to increased activity by the rays, but more likely that their greater number at this stage of reaction represents a phase in the regeneration of lymphocytes. That this phase is transient is shown by the circumstance that, as soon as lymphocytic regeneration has progressed to a certain point, the epithelioid cells disappear. Primary, direct increase in the number or activity of cells can occur as a transient phase of reaction, but it cannot be maintained for more than a short time, after which the

cells either return to their normal state and number or disintegrate. Neither Stephan nor anyone else has been able to prove that roentgen or radium rays, under any conditions of dosage, can directly increase the number or metabolism of cells for any length of time. Murphy and his coworkers have apparently shown that the mitotic activity of lymphocytes can be increased by exposure to small doses of roentgen rays, but their experiments do not prove that the multiplication of lymphocytes is a primary and direct effect of irradiation. Indirect or secondary increase in cells, on the contrary, is a common result, but, as far as our present knowledge indicates, always implies antecedent destruction of cells of the same or of some other kind.

When the comparative effect of small and large doses is considered, it becomes necessary to lean heavily upon Einstein. It is amazing how much of ambiguity the words "small" and "large," or "weak" and "heavy," may contain when they are used to qualify the word "dose," as applied to roentgen rays or radium. Küpferle, Bacmeister, De la Camp, and other disciples of the Freiburg school, have usually employed moderately strong doses. As far as may be judged from the technical data furnished, the quantity of rays was not sufficient to cause radiodermatitis and hence must be classed as suberythemal. Manoukhin, Fränkel, Verdun and Dausset, Trémolières and Colombier, and Stephan, on the contrary, advocated small doses to the spleen alone or to the spleen and long bones; they did not specify clearly what they meant by small doses, but implied doses representing a fraction smaller than one-half or one-third of the erythema dose. To pretend that such doses stimulate but do not destroy cells is to abuse the word "stimulate" and disregard an important mass of experimental and clinical facts. As has been repeatedly shown, the radiosensitiveness of lymphocytes is such that the smallest dose of roentgen rays used for therapeutic purposes, when directed to an organ containing lymphoid tissue or circulating leucocytes, can cause the destruction of a certain proportion of lymphocytes; the polymorphonuclear cells are somewhat less sensitive. Therefore, the protagonists of the small dose method are treading on thin ice when they rest their contention on the importance of avoiding cellular destruction. Moreover, the polymorphonuclear leucocytosis noted after irradiation by Verdun and Dausset, Trémolières and Colombier, and others, cannot be accepted as characterizing the action of roentgen rays on tuberculosis, because, as is well known, it is only a transient phase in the reaction of blood corpuscles to roentgen and radium rays. Twelve to twenty-four hours after exposure of the entire body of normal rats, guinea pigs, rabbits, or of a large area of the trunk of a human being, a sharp increase in the number of polymorphonuclear cells has often been noted; this phase of polymorphonuclear leucocytosis is only transient, however, and is rapidly followed by leucopenia lasting from a few days to three weeks or even longer.

Another point which must be borne in mind is that the results obtained with large or small doses, or by irradiating the lungs or the spleen, the lungs and spleen, the lungs, spleen and long bones, or only the spleen and long bones, appear to be about the same. This can mean only one of two things: either exposure to the rays had nothing to do with the supposed improvement or cure, which was due to other factors and would have occurred in any event, regardless of irradiation; or the action of the rays was much the same, irrespective of the organ or territory exposed to them. The effects of irradiation noted in some of the experiments on animals and those described by numerous clinicians following irradiation of patients with pul-

monary tuberculosis correspond so closely in character to the changes in tuberculous lymph nodes which roentgen rays are known to induce that it would be difficult to reject the former and accept the latter as authentic. And yet, as PARRISIUS (1926) has brought out, it may be that the favorable effects ascribed to irradiation were such as might have occurred without irradiation, because the cases in which they were observed were precisely those in which changes of this kind may take place spontaneously or after treatment by other methods, that is to say, in cases which have a natural tendency to heal.

Granting that improvement or cure was actually due to irradiation, at least in part, what rôle did radiation play and how were the favorable alterations brought about? In all probability, the primary effect of the rays was to destroy lymphocytes infiltrating the tubercles. The greater the degree of leucocytic infiltration, the greater the lymphocytic destruction; hence, the greater the influence of irradiation during the early stages of the nodular form of the disease, and least the effect of the rays when infiltrating leucocytes had been largely or wholly replaced by caseous material or connective tissue, with or without calcification. The increase in phagocytosis which follows disintegration of lymphocytes and by which the cellular débris is disposed of, as well as the liberation of antibodies from the destroyed cells and perhaps also the simultaneous action of lipolytic or other ferments, may assist in destroying the offending bacilli and in producing a reaction the result of which is increased proliferation of connective tissue cells and sometimes calcification. The proportion of connective tissue in the tubercles probably accounts for the necessity of repeated irradiation in tuberculosis as in other chronic inflammatory conditions, whereas in acute inflammations a single exposure is often sufficient to induce complete resolution. As far as the quantity of roentgen rays is concerned, small or moderate doses are preferable to full, tolerance doses.[183] Indeed, doses of the order of those employed in dealing with neoplasms, in which maximum destruction of tumor cells is the main objective, are not only less effective but actually dangerous, because to superimpose on the tuberculous inflammation an additional inflammatory reaction from excessive irradiation is to interfere with the existing defense against tuberculosis and perhaps to disseminate the infection even more widely.

Roentgen Injury to Pleura and Lungs. The first mention of possible irritation of the pleura and lungs by radiation, which I have been able to find, was made by JESSEN and RZEWUSKI (1909–1910), who, writing about radiotherapy for pulmonary tuberculosis, stated that repeated exposures to from 30 to 36 milliampere-minutes of roentgen rays corresponding to 5 Benoist[184] caused increased cough, expectoration, and fever, followed by recession of these symptoms. But since Jessen and Rzewuski irradiated lungs already diseased, it is impossible to be certain that the increased manifestations of pulmonary abnormality were a direct effect of irradiation. STRASSER (1912) reported the instance of a patient aged sixty-eight years, with a tumor in the upper part of the mediastinum, who had been irradiated four times over the thorax and neck and who, after the third exposure or series of exposures, presented symptoms and physical signs of mediastinal pleuritis (anginoid pain, fever and friction rub). On roentgenologic examination, the mediastinal tumor was found to have disappeared. A review of the sequence of events leads to the conclusion that

[183] In the sense of fractions or the whole of an erythema dose.
[184] Benoist radiochromometric scale.

the disappearance of the neoplasm probably resulted from the destructive influence of the rays on its cellular elements, and that the destroyed cells were replaced by fibrous tissue which may have contracted sufficiently to cause pain. This explanation is only partly satisfactory, however, because the fever and friction rub appear to have been manifestations of pleuro-pulmonary inflammation. In the absence of more detailed information, it is impossible to be certain whether or not this case should be regarded as an example of pleuropulmonary reaction to roentgen rays.

Groover, Christie, and Merritt (1922) apparently were the first to give unmistakable evidence of pulmonary reaction to roentgen rays when they reported having treated the thorax of a considerable number of patients for cancer of the breast with rays generated at moderate voltage and filtered through 0.5 mm. of copper and 1.0 mm. of aluminium to the point of deep bronzing, vesication, and subsequent desquamation of the skin. Some of these patients developed infiltrative changes in the lungs, beginning at the hilus, spreading outward into the lung, and accompanied by dyspnea. The symptoms included an irritative, unproductive, and usually paroxysmal cough arising three or four weeks after exposure to the rays, that is, at about the time when inflammatory reaction of the overlying skin became apparent. Soon thereafter, roentgenologic signs of pulmonary infiltration at or near the hilus could be perceived; during the next three or four weeks, the infiltration extended rapidly until practically the entire lung was involved, and this was accompanied by dyspnea. The roentgenographic features suggested those of influenzal pneumonia. Because the condition of the patients was better than could have been expected if the pulmonary lesions had represented metastatic invasion and because the infiltration spread rather too rapidly for metastasis, Groover, Christie and Merritt perspicaciously deduced that the pulmonary inflammation was directly related to irradiation. Definite pulmonary fibrosis was found later in one patient, and this was regarded as substantiating their previous impression; in the other patients, pulmonary infiltration disappeared without leaving any traces. All these patients had been exposed to rays generated at a potential equivalent to a parallel spark-gap of from 8.5 to 9.5 inches, filtered through 0.5 mm. of copper and 1 mm. of aluminium, at a focal-skin distance of 12 inches, for three hours (each field). Hines (1922) reported two cases, in which he thought roentgen rays had probably caused reactive inflammation of the lungs, but the circumstances and necropsy findings were such that Hines' interpretation hardly seems warranted. All the changes described may have been related to multiple metastatic foci in the lungs and pleura. Tyler and Blackman (1922) confirmed the opinion of Groover, Christie, and Merritt by recording seven cases (six cases treated for carcinoma of the breast and one for carcinoma of the thyroid gland), in which inflammation of the pleura and lungs was thought to be related to irradiation, and this deduction was supported by the physical signs and roentgenologic features. Groover, Christie, and Merritt (1923) described an additional case in which cough and dyspnea appeared synchronously with cutaneous erythema after irradiation of the thorax, and evidence of pulmonary fibrosis with adhesive pleuritis was obtained later. It was their impression that these manifestations of pulmonary reaction were related to the use of copper filters which, by absorbing the long wave-length components of the beam of radiation emitted by the tube, increased the penetrating power of the remaining rays. Desjardins (1923) cited a clear example of roentgen pleuropneumonitis, and

Davis (1923) presented three additional cases, including that reported by Desjardins; the authenticity of these appears unassailable. Many other authors, such as Case (1922), Rose (1923), Wintz (1923), Cathcart (1923), Bissell (1923), and Mühlmann (1924), have mentioned similar examples of reaction of the lungs to excessive irradiation.

It is interesting that the possibility of inducing pleuropulmonary inflammation by exposing the thorax to strong doses of roentgen rays did not attract attention until treatment with rays of short wave-length came into use. This, no doubt, was largely attributable to the doctrine of the so-called "carcinoma dose" and the consequent vogue of doses which exceeded the limit of tolerance of the skin of the thorax. Most of the cases of acute or chronic pleuropneumonitis from irradiation occurred in women with cancer of the breast, who had undergone radical amputation of the affected mammary gland and had been irradiated repeatedly to prevent recurrence. A few of the cases observed, however, had received thoracic irradiation for other conditions. The reports of Groover, Christie, and Merritt and of Tyler and Blackman spread the impression that such reaction of the pulmonary structures occurred only after irradiation of the thorax with rays filtered through copper, which is to say with rays of relatively short wave-length. Subsequently, Evans and Leucutia (1925), Desjardins (1926), and Groover, Christie, Merritt and Coe (1927) were able to correct this erroneous impression by showing that the same reaction can be produced by roentgen rays of medium or short wave-length, and that the essential factor is the quantity and not the quality of the rays. Groover, Christie, Merritt and Coe made it clear that any factor which increases the quantity of rays reaching the lungs, such as increase in electrical potential, in filtration, in focal-skin distance, in areas of surface exposed, and in time of exposure, increases the tendency to pleuro-pulmonary reaction. The thickness of the thoracic wall was rightfully mentioned as another important factor, and conditions favoring physiological or mechanical atelectasis were held as predisposing elements; but, as was emphasized by Desjardins, the time of exposure is far the most important single element. Like other organs, the lungs can readily tolerate roentgen rays up to a certain limit, but reactive inflammation may ensue when such limit is exceeded. Therefore, to expose the thin thoracic wall of women who have undergone radical amputation of a breast, or of other patients with thoracic walls naturally thin or made so by emaciation, to doses of roentgen rays sufficient to induce more than a faint erythema of the skin, especially if such exposure is repeated, is to risk causing more or less severe reaction of the pulmonary structures.

Roentgen pleuropneumonitis begins as an acute inflammation of the pleura and lungs in the region excessively irradiated. The clinical manifestations of such inflammation may be mild and consist of cough and slight dyspnea, or severe and characterized by a distressing, unproductive and often paroxysmal cough, rapid respiration, marked dyspnea, increase in pulse rate, weakness, pain and fever. As Groover, Christie, and Merritt pointed out, the onset of symptoms is synchronous with the appearance of cutaneous erythema; indeed, they never observed pulmonary reaction unless distinct erythema of the skin, usually to the second degree, also was manifest. Symptoms as well as physical and roentgenologic signs of pulmonary disturbance appear three or four weeks after irradiation, but may not attract attention until some time later. Usually the patient thinks she has acquired an ordinary

"cold," and the attending physician himself may be deceived. The physical signs are usually limited to one lung, on the side of the amputation in the case of cancer of the breast, or on the side receiving the strongest dose in other diseases. Dry and moist râles, pleural friction rub, evidence of pulmonary infiltration and sometimes of slight pleural effusion, may be elicited in the more severe grades of inflammation. As the acute manifestations recede, the physical signs may disappear completely and no perceptible abnormality may remain; or the physical signs may diminish and chronic adhesive pleuritis and pulmonary sclerosis, with a measure of functional impairment, may persist. The roentgenologic features consist in diminished expansion of the affected half of the thorax on one or both sides, elevation and immobility of the diaphragm, displacement of the heart and mediastinum toward the affected side, a foggy appearance of the parenchyma adjacent to the hilus, rapid outward extension of the pulmonary infiltration represented by an irregular or patchy area of increased density, and compensatory emphysema of the opposite lung when this also is not involved. The acute phase usually subsides in from one to three weeks, but the cough, rapid respiration and dyspnea may persist for weeks or months. Except during the acute stage, the general condition of the patient is not greatly influenced, as a rule, but the dyspnea may force her to curtail her activities. In mild cases the symptoms disappear in a short time, but if the patient is subjected to further roentgenization at full dosage, they may return in a more severe form, and cough, dyspnea, increased pulse rate, and weakness may continue indefinitely. The infiltration may be rapid and then clear up progressively, or the process may extend for a longer time, in which event the pulmonary changes are more likely to leave permanent marks. Expansion of the affected lung and mobility of the corresponding leaf of the diaphragm may be restricted permanently, retraction of the heart may persist, and cough and breathlessness may continue indefinitely. Naturally, the site of infiltration must depend on the conditions of irradiation, and cause and effect must coincide in the same region. Similar symptoms, physical signs, and roentgenologic indications in a patient who has never been exposed to roentgen rays, or who has been exposed to doses insufficient to induce such reaction, obviously cannot be due to irradiation and must be ascribed to some other cause.

Depending on the degree of excess in dosage, pleuropneumonitis may follow a single exposure or series of exposures, or may not appear until the patient has been irradiated two or more times at intervals of three or four weeks. In fact, under ordinary therapeutic conditions, such reaction occurs only in a small percentage of patients and may be avoided entirely by the simple expedient of reducing the quantitative dose per field or by increasing the interval between successive courses of treatment. Referring specifically to roentgen rays generated at a potential of approximately 200 kilovolts, Evans and Leucutia stated that, if less than 100 per cent of the skin unit dose is given to the thorax at one time, inflammatory reaction of pleura and lung will not ensue, but if a dose greater than 100 per cent is given, reaction may occur. If the dose does not exceed 130 or 140 per cent of the skin unit dose, the reaction will appear as pulmonary infiltration, usually disappearing in from six to nine months following exposure. When the thorax is exposed to more than 140 per cent of the skin unit dose, pulmonary infiltration may be replaced by connective tissue sclerosis. With rays generated at a maximum potential of 135 kilo-

volts and filtered through 6 mm. of aluminium, Desjardins has observed some degree of pleuropneumonitis in about 2.5 per cent of several hundred patients, in which the thorax was irradiated for 40 or 45 minutes (800 r to 1000 r in air), but has never seen such reaction after exposure for thirty minutes (600 r in air), even when repeated several times at intervals of three or four weeks. Nevertheless, when the patient is a small individual with thin thoracic wall or when the same territory must be irradiated several times, the surface dose per field is reduced to between 500 and 600 r in air; this is especially important when several beams of rays are made to converge on the underlying lung.

CONCLUSIONS

Nose

The radiosensitiveness of the mucous membrane of the nose and its accessory sinuses has not been determined experimentally, but there is reason for believing that it does not differ much in this respect from the mucous membrane of the mouth, pharynx and larynx, the sensitiveness of which varies only to a limited extent in different portions.

Radiotherapy may exert a beneficial influence in a certain proportion of cases of acute and chronic sinusitis (maxillary and frontal sinuses), and of polypoid sinusitis.

In hay fever and ozena the value of roentgen or radium irradiation has not been clearly established, but on rhinoscleroma and tuberculosis of the nasal mucous membrane roentgen rays and radium appear to have a distinctly favorable effect.

Only one instance of supposed radiation injury to the nose has been recorded, but its authenticity is doubtful.

Larynx

The radiosensitiveness of the mucous membrane of the larynx is approximately the same as that of the oral mucosa, although, as determined clinically by Coutard, slight variation in different parts of this structure must be allowed.

Experiments on a small number of animals indicate that roentgen rays have a definite, though limited, action on tuberculosis of the larynx and increase the tendency of such lesions to heal. The rays apparently cause a certain proportion of the infiltrating leucocytes (notably the lymphocytes) to disintegrate and to liberate antibodies and ferments. This is probably followed by phagocytosis of degenerated leucocytes, increased lysis and phagocytosis of the infecting bacteria, and replacement of the destroyed cells by connective tissue.

The therapeutic value of roentgen irradiation for laryngeal tuberculosis has been demonstrated, but should not be employed exclusively. Other methods of proved worth, such as rest, dietetic and meteorologic conditions, and natural or artificial heliotherapy in suitable cases, should be used in conjunction.

Roentgen rays also have yielded favorable results in blastomycosis of the larynx.

Excessive irradiation of the larynx (roentgen rays or radium) may cause an inflammatory reaction characterized by redness and edema of the mucosa, with focal necrosis of the laryngeal cartilages; even several months or years later, these disturbances may be accompanied or followed by stenotic thickening and dyspnea,

and in some cases by pneumonia and death. Many examples of such reaction have been reported.

Lungs

Experiments on animals have proved fairly conclusively that the radiosensitiveness of the pleura and lungs is approximately the same as that of the overlying skin, and that a dose of roentgen rays sufficient to cause an inflammatory reaction in the skin of the chest, especially when the thoracic wall is thin or when it is irradiated repeatedly at comparatively short intervals, is prone to induce inflammatory changes in the pleura and lungs. The mucus-secreting cells of the epithelium lining the bronchi and of the mucous bronchial glands are more radiosensitive than other epithelial cells and are the first to react by undergoing mucoid degeneration and pouring out an increased quantity of mucus for a time, but later the quantity of secreted mucus diminishes. This is followed by catarrhal bronchitis, with desquamation of bronchial epithelial cells, and bronchopneumonia in the irradiated portion of the lung. As a result of secondary infection, the bronchial inflammation often assumes a purulent character and is readily transmitted to other animals. The pleuropneumonitis may manifest itself at about the same time as the inflammatory reaction in the overlying skin, but this depends on the radiosensitiveness of the skin of each species of animal. Other experiments seemed to show that roentgen irradiation of the lungs at extremely short range causes an initial increase, followed by a marked decrease, in the rate of respiration, but this was found to be due to high-tension electrical discharges, and not to radiation.

External exposure of the entire body to a large quantity of radium may induce extensive degeneration of leucocytes, especially lymphocytes in the spleen, lymph nodes, intestinal lymph follicles and bone marrow, mucoid degeneration of the epithelium and hyperemia of the intestine, cellular degeneration in the testis or ovary, stomach and intestine, kidneys and liver, mucoid degeneration and desquamation of the columnar epithelium of the bronchi and trachea, hyperemia, alveolar exudation, and focal consolidation of the lungs.

Intravenous or oral administration of sufficient doses of thorium X induces a leucopenia affecting chiefly the lymphocytes, large mononuclear cells, and blood platelets, hyperemia and hemorrhage of the bone marrow, marked destruction of lymphocytes and atrophy of lymphoid follicles in the spleen and lymph nodes, inflammation and destruction of the vascular endothelium, with secondary proliferative thickening of the vessel walls, central parenchymatous necrosis of the lobules of the liver, hyperemia, exudative distention of the glomerular capsules and coagulation necrosis of the kidneys, and intense hyperemia of the lungs, with exudative distention of the alveoli. After intravenous injection, the greatest changes appear to be in the blood vessels, lymphoid structures, and liver, whereas, after oral ingestion, the large intestine, lymphoid structures, and kidneys suffer the greatest injury.

Irradiation is of distinct value in pneumonia and delayed pneumonic resolution, its action apparently depending on the relative proportion of infiltrating leucocytes and organization.

Many physicians have claimed a favorable influence of radiotherapy for whooping cough, and long series of cases have been recorded as tending to establish its value; nevertheless, the beneficial effect of irradiation has not been conclusively proved and a measure of doubt persists.

In a considerable percentage of cases of bronchial asthma and chronic asthmatic bronchitis, roentgen irradiation of the lungs and mediastinum, the spleen, the lungs and spleen, or other parts of the body, may cause the crises to disappear for a short or long time. The rays apparently act by destroying leucocytes, especially lymphocytes, in the irradiated territory, and the cellular disintegration probably induces a sort of autogenous protein reaction.

As in other organs, echinococcus cyst of the lung is not appreciably influenced by roentgen irradiation.

Exposure of the lungs, and sometimes of the spleen, to moderate doses of roentgen rays may have a definite effect on pulmonary tuberculous lesions, may retard the evolution of the tubercles, diminish the tendency to caseation and to perituberculous pneumonitis, increase the proliferation of connective tissue and hasten calcification, probably according to the relative proportion of infiltrating leucocytes and connective tissue at the time of irradiation. This is especially true in the early, infiltrative stage of the tubercles in the chronic, productive form of the disease. The inability of some investigators to observe such effects may have been due to excessive irradiation or to rapid dissemination of infection when the bovine type of *Mycobacterium tuberculosis* was used. Under proper conditions and in well selected cases, roentgen therapy may be distinctly valuable, but it should be restricted to institutions, where it may be used in conjunction with other well established methods of treatment. Here again, the action of the rays seems to depend on destruction of infiltrating leucocytes and on the proportion of connective tissue.

Excessive irradiation of the lungs (either too large a quantitative dose at one sitting, in several sessions at intervals, or by reason of the convergence of two or more beams of rays) may induce an inflammatory reaction of the pleura and lungs which, if slight, may disappear or which, if severe, may lead to adhesive pleuritis and scarring of the lung, with more or less functional disability.

To be Continued.